(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



| 1311 | 1312 | 1313 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314 | 1314

(43) International Publication Date 16 August 2001 (16.08.2001)

PCT

(10) International Publication Number WO 01/58951 A2

(51) International Patent Classification7:

C07K 14/705

(21) International Application Number: PCT/EP01/01457

(22) International Filing Date: 9 February 2001 (09.02.2001)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

00200443.0 00203810.7 10 February 2000 (10.02.2000) EP 31 October 2000 (31.10.2000) EP

(71) Applicant (for all designated States except US): STICHT-ING VOOR DE TECHNISCHE WETENSCHAPPEN [NL/NL]; Van Vollenhovenlaan 661, NL-3527 JP Utrecht (NL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SMIT, August, Benjamin [NL/NL]; Achillesstraat 28 II, NL-1076 RC Amsterdam (NL). SIXMA, Titia, Karen [NL/NL]; Ingen Houszstraat 61, NL-3514 HV Utrecht (NL).

74) Agent: VOSSIUS & PARTNER; Siebertstr. 4, D-81675 München (DE).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

 without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: WATER-SOLUBLE LIGAND-BINDING PROTEINS AND ANALOGS OF LIGAND-GATED ION CHANNELS, CRYSTALS THEREOF AND THEIR USE FOR SCREENING LIGANDS OF LIGAND-GATED ION CHANNELS

(57) Abstract: Provided are water-soluble ligand-binding proteins derived from molluscs and analogs of ligand-gated ion channels, crystals thereof and their use for screening ligands of ligand-gated ion channels. In particular, water-soluble ligand-binding proteins are provided that are capable of forming multimers and are amenable to crystallization. The crystal structure of one of these proteins, an acetylcholine binding protein (AChBP) is provided, which can be used to generate 3D models of the extracellular ligand-binding domain of ligand-gated ion channels and thus for screening of drugs that act on these ion channels. Furthermore, chimeric proteins are provided that are capable of binding a ligand of a ligand-gated receptor, and comprising at least the amino acids of the AChBP determining solubility of the AChBP, in the same positions as in the AChBP, and furthermore comprising amino acids determining binding to said ligand.

WATER-SOLUBLE LIGAND-BINDING PROTEINS AND ANALOGS OF LIGAND-GATED ION CHANNELS, CRYSTALS THEREOF AND THEIR USE FOR SCREENING LIGANDS OF LIGAND-GATED ION CHANNELS

10

15

20

25

5

SUMMARY OF THE INVENTION

Novel water-soluble ligand-binding proteins have been identified and isolated, which have a ligand-binding profile substantially similar to that of ligand-gated ion channels. DNA molecules encoding such proteins have been cloned and characterized. The biological and structural properties of these proteins are disclosed, as is the amino acid and nucleotide sequence. The recombinant DNA molecules, and portions thereof, are useful for isolating homologues of the DNA molecules, identifying and isolating genomic equivalents of the DNA molecules, and identifying, detecting or isolating mutant forms of the DNA molecules. Using a recombinant expression system functional DNA molecules encoding the water-soluble ligand-binding proteins as well as chimeras have been functionally produced. Furthermore, the water-soluble ligand-binding proteins could be crystallized revealing the three dimensional (3D) structure and enabling the modeling of the 3D structure of the ligand-binding domain of ligand-gated ion channels. The invention is further in the field of the development of new drugs that are capable of selectively intervening in neuronal signaling pathways. The invention is more in particular concerned with providing new analogues of the channel-coupled receptors, crystal structures thereof and to their use in screening ligands for these receptors.

30 Several documents are cited throughout the text of this specification either by name or are referred to by numerals within parenthesis. Full bibliographic citations may be found at the end of the specification immediately preceding the claims. Each of the documents cited herein (including any manufacturer's specifications, instructions, etc.) are hereby incorporated herein by reference; however, there is no admission that any document cited is indeed prior art as to the present invention.

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

BACKGROUND OF THE INVENTION

The communication in the central nervous system (CNS) occurs through a complex interaction of electrical and chemical signals. Molecules bearing chemical information are called neurotransmitters. The chemical information is converted in electric currents on the post-synaptic membrane, which is specialised in recognising and binding neurotransmitters by means of protein receptors. The specific binding of a ligand to one type of such receptors, the ionotropic receptors, induces a fast opening of the ion channel coupled to the receptor. An important group of ionotropic receptors is the superfamily of the channel-coupled receptors, also referred to as ligand-gated receptors, including the 7-amino-butyric acid (GABAA) receptor, the glycine receptor, the serotonin-3 (5-HT3) receptor and both neuronal and muscle-type nicotinic acetylcholine receptors (nAChR). These receptors share certain structural features such as (1) a 15-residue cysteine loop between amino acids 128 and 142 corresponding to the Torpedo AChR α unit, (2) four trans-membrane domains. (3) similar subunit arrangements, and (4) homologies in amino acid sequence. Activation of these receptors causes a change in electrical current and hyperpolarisation of the cell membrane and consequently an inhibition of the electrical activity of the cell. The GABA_A receptor and the glycine receptor are coupled to a chloride-selective channel. and thus the inhibition of the electrical activity leads to inhibition of the cell response. On the other hand, activation of the 5-HT3 receptor and the nAChRs provokes an excitatory response on the cell because they are connected to a cation-selective channel (Na+, K+, Ca2+). The AChRs are the best studied of the ligand-gated receptors; for a review, see Arias, Brain Research Reviews, 25 (1997)133-191 and Arias, Neurochem. Int. 36 (2000), 595-645). Mutations in these ligand-gated ionchannels (LGICs) lead to diseases such as congenital myasthenia gravis, epilepsy, startle syndrome and alcohol sensitivity (Vafa and Schofield, Int. Rev. Neurobiol. 42, 285-332; 1998). NAChRs mediate nicotine addiction in chronic tobacco users. Since nicotine binding to these receptors also has a positive effect on Alzheimer's disease. Parkinson's disease and schizophrenia these receptors present an important drug target (Paterson and Nordberg, A. Neuronal nicotinic receptors in the human brain. Prog. Neurobiol. 61, 75-111; 2000).

The development of new active compounds that can selectively or - as the case may be - a-selectively bind to the channel-coupled receptors, is of utmost importance for the understanding of the processes occurring in the nervous system and for the treatment of disturbances of neural conditions. The development of such active compounds requires the availability of a reliable model system for the corresponding receptors. The primary structural features (amino acid sequences) of the various

PCT/EP01/01457

WO 01/58951

5

15

20

25

30

35

-3

receptors have been largely elucidated by now. Certain subunits of the AChRs have been found to be determinant in the pharmacological specificity or affinity of the receptor for its ligand (Corringer et al., J. Neuroscience 18 (1998), 648-657). However, the study of the ligand binding properties of the receptor proteins is hampered by the fact that the spatial structure of the proteins - which is decisive in the binding of ligands - is still unknown. This is partly because crystallisation of the receptor proteins has been unsuccessful up to now.

The above-defined technical problem is solved by the present invention by providing the embodiments characterized in the claims.

Accordingly, in one aspect the present invention relates to a water-soluble protein derived from a mollusc being capable of binding a ligand of a ligand-gated receptor.

It has been found according to the invention that acetylcholine-binding proteins (AChBP) of certain molluscs show a surprising structural similarity with the channel-coupled receptors on the one hand and have interesting physical properties, such as water-solubility, on the other hand. The molluscan AChBPs are capable of forming multimers, especially pentamers, and of binding specific toxins such as α -bungarotoxin. These multimers may be homogeneous (identical units) or heterogeneous (different units). These properties make them eminently suitable as model systems for studying the binding of candidate ligands to the channel-coupled receptors. It has been possible to produce these molluscan AChBPs in recombinant systems, thus allowing convenient and large-scale production thereof. Moreover, it is feasible to construct hybrid proteins sharing the physical properties of the mollusc AChBP with the pharmacological properties of the (human) channel-coupled receptors, thus providing new dedicated tools for screening ligands for these receptors.

The AChBP is a naturally occurring analogue of the extracellular domains of the α -subunits of the neuronal nicotinic acetylcholine receptors (nAChRs). In contrast to the nAChRs, it lacks domains to form a transmembrane ion channel, but alike the nAChRs it assembles into a homo-pentamer (Figure 6). Moreover, AChBP has ligand-binding characteristics that are typical for a nicotinic receptor. The 3-dimensional structure of AChBP was solved by X-ray crystallography at 2.7Å resolution (current R_{tactor} = 27.9 %, R_{tree} = 30.0 %). In crystals, as in solution, AChBP forms a stable homo-pentamer with dimensions comparable to those of the ligand-binding domain of the nAChR, as determined in EM studies by Unwin, Struct. Struct. Biol 121 (1998), 181-190. The high-resolution crystal structure of AChBP, along with

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-4

biochemical and pharmacological data, supports the extrapolation of AChBP as a good mimic of ligand-binding domains of ligand-gated ion channels including nAChR, 5-HT3R, GABA_{AC}R and GlyR.

Four AChBPs according to the present invention are exemplified herein, isolated and cloned from the CNS of Lymnaea stagnalis (L-AChBP_T1 and L-AChBP_T2) and Bulinus truncatus (B-AChBP_T1 and B-AChBP_T2). L-AChBP_T1 and 2 are 229 amino acid proteins with a signal sequence of 19 amino acids (224 and 21 amino acids, respectively, for B-AChBP_T1 and 2; see also Figure 1) and have sequence homology with the extracellular domains of the subunits of ligand-gated ion channels (Figure 3), in particular with those of the nAChRs (Figure 4 and 5). The mass of the purified AChBP from Lymnaea has been determined by mass-spectrometry. The glycosylated form has a mass of about 24720 Da and the de-glycosylated form of about 23832 Da. In SDS-PAGE the glycosylated AChBP migrates between the 14 and 26 kDA marker proteins. Hydrophopicity plots of the AChBPs are shown in Figure 2, which reveal those regions of the ligand-binding proteins that are particularly hydrophilic and thus may be replaced at least in part or essential amino acids thereof in the ligand-binding domain of the ligand-gated ion channel. Sequence conservation is particularly high in the so-called loop areas (reviewed by Arias, Neurochem. Int. 36 (2000), 595-645), which contain the residues involved in ligandbinding. The cysteine residues characteristic for the Cys-loop family of ligand gated receptors are conserved in AChBP. Also the double cysteine typically found in the alpha subunits of the nAChR is present. AChBP protein sequence ends at the position where in the nAChRs the first predicted transmembrane domain would start. The ligand-binding characteristics of AChPBs are described in Example 4 and summerized in Table 2.

The terms "channel coupled receptors", "ligand-gated receptor", "ligand-gated ion channel" are used interchangeable herein. However, in context with the natural occurring, in particular human molecules the term "ligand-gated ion channel" is preferably used. The water-soluble ligand-binding protein of the invention can also be characterized as a ligand-binding protein having at least 10%, more preferably at least 12%, still more preferably at least 15% and most preferably at least 20% amino acid sequence identity to a vertebrate ligand-gated ion channel but missing any trans-membrane domain. A ligand-gated receptor of the present invention is characterized by having substantially the same ligand-binding characteristics of a vertebrate, preferably mammalian, most preferably human ligand-gated ion channel but comprising at least one alteration in the original amino acid sequence, said

20

25

30

35

WO 01/58951 PCT/EP01/01457

-5

alteration resulting in the presence of an amino acid determining or contributing to the water-solubility of the water-soluble ligand-protein found in molluscs, in particular snails such as those described in more detail below.

The terms "ligand-binding protein", "ligand-binding domain" and "ligand-binding receptor" are meant to at least include the portion of a water-soluble ligand-binding protein or corresponding modified ligand-gated ion channel required for binding a ligand. Minimally the ligand-binding domain consists of a peptide containing that domain. However the use of this term is meant to include a ligand-binding domain or protein that is comprised by a larger portion of, for example, ligand-gated ion channel, such as a fully reconstituted nicotinic acetylcholine receptor.

As shown in Figure 3 the nicotinic acetylcholine receptor (nAChR) belongs to a well-understood member of the ligand-gated ion channels superfamily. The members of this signaling protein group, including 5-HT3, glycine, GABA_A, and GABA_C receptors, are thought to share common secondary, tertiary, and quaternary structures on the basis of a high degree of sequence similarity. Therefore, it is expected that the novel findings in respect to the exemplified AChBP equally apply to the other members of the mentioned ligand-gated ion channels superfamily. Thus, either water-soluble protein being capable of binding a ligand of any of those ligand-gated ion channels may be found in molluscs or the present 5-HT3, GABA_A, and glycine receptors can be modified such as to substantially retain their binding affinity.

Accordingly, the ligand of the water-soluble ligand-binding protein is preferably acetylcholine, gamma-amino-butyric acid (GABA), glycine, nicotine or serotonin. Isolation of such water-soluble ligand-binding proteins can be done as described in Example 1 for the AChBP of the present invention. Instead of α -bungarotoxin other known ligands or can be used for affinity purification. Most preferably, water-soluble ligand-binding protein of the invention is a acetylcholine-binding protein (AChBP). Preferably, the ligand-binding protein displays substantially the binding characteristics shown in Table 2.

The acetylcholine-binding proteins to be used according to the invention are originally derived from aquatic molluscan species, especially species from the class of the snails (Gastropoda), in particular from the order of the lunged snails (Pulmonata). The order of the Pulmonata is divided into the suborders of the Basommatophora (mostly aquatic snails), Systellommatophora and Stylommatophora (mostly land snails). The Basommatophora include the families of the Acroloxidae (e.g. genus Acroloxus), Lymnaeidae (e.g. genera Galba, Stagnicola, Radix and Lymnaea),

15

25

30

35

WO 01/58951 PCT/EP01/01457

-6

Physidae (e.g. genera Physa and Aplexa) and Planorbidae (e.g. genera Planorbis, Anisus, Ancylus, Gyraulus, Biomphalaria and Bulinus). Examples of suitable species are *Lymnaea stagnalis* (pond snail) and *Bulinus truncatus*. The isolation of the AChBPs from these snails, cloning of the cDNA encoding these AChBPs and their characterization including the full amino acid sequences is described in the examples. The cDNA and amino acid sequences of the AChBPs of *Lymnaea stagnalis* are depicted in SEQ ID Nos. 1 and 2 (L-AChBP_T1) and SEQ ID Nos. 3 and 4 (L-AChBP_T2). Those of *Bulinus truncatus* are depicted in SEQ ID Nos. 5 and 6 (B-AChBP_T1) and SEQ ID Nos. 7 and 8 (B-AChBP_T2). Features of these proteins are further described in the examples and the accompanying figures.

While a water-soluble ligand-binding protein derived form a Pulmonata species, preferably from a Basommatophora species is preferred, it will be appreciated that the present invention generally relates to any water-soluble protein being capable of binding a ligand of a ligand-gated receptor comprising an amino acid sequence selected from the group consisting of:

- (a) an amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4,
 6 or 8 or a functional equivalent thereof, or a fragment of at least 5
 continuous amino acids thereof;
- 20 (b) an amino acid sequence having at least 30% amino acid identity to the amino acid sequence of any one of SEQ ID Nos. 2, 4, 6 or 8; and
 - (c) an amino acid sequence resulting in a protein which is detectable by a monoclonal or polyclonal antibody which recognises, preferably with a binding affinity of at least 10⁻⁷M, a protein comprising an amino acid sequence of (a) or (b).

Identity or similarity, as known in the art, are relationships between two or more polypeptide sequences or two or more polynucleotide sequences, as determined by comparing the sequences. In the art, identity also means the degree of sequence relatedness between polypeptide or polynucleotide sequences, as the case may be, as determined by the match between strings of such sequences. Both identity and similarity can be readily calculated (Computational Molecular Biology, Lesk, ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part I, Griffin and Griffin, eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, Academic Press, 1987; and Sequence Analysis Primer, Gribskov and Devereux, eds., M Stockton Press, New

-7

York, 1991). While there exist a number of methods to measure identity and similarity between two polynucleotide or two polypeptide sequences, both terms are well known to skilled artisans (von Heinje, supra; Gribskov and Devereux, supra; and Carillo and Lipman SIAM J. Applied Math. 48 (1988), 1073). Methods commonly employed to determine identity or similarity between sequences include, but are not limited to those disclosed in Carillo and Lipman; see supra. Preferred methods to determine identity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer programs. Preferred computer program methods to determine identity and similarity between two sequences include, but are not limited to, GCG program package (Devereux et al., Nucleic Acids Research 12 (1984), 387), BLASTP, BLASTN, psi BLAST and FASTA (Atschul et al., J. Molec. Biol. 215 (1990), 403).

In another embodiment, the present invention relates to a water-soluble protein being capable of binding a ligand of a ligand-gated receptor comprising

- (a) at least the amino acids of the water-soluble protein described above determining solubility of said protein, in the same or corresponding positions as in said protein; and
- (b) at least 4 amino acids determining binding to said ligand.

20

25

30

35

5

10

15

Protein expression studies have shown that wild-type AChBP of the mollusc Lymnaea stagnalis can be produced in Pichia pastoris yeast. The yeast cells express AChBP in a homopentameric form and secrete the protein complex into the medium. The large amounts of AChBP per volume of medium produced (up to 2 mg per liter medium) and the large volumes of yeast that can be cultured allow a large-scale production of AChBP. Besides the wild-type AChBP, various AChBP mutants have been produced in Pichia pastoris. These include mutants containing the following single point mutations (the numbers refer to the amino acid position in the AChBP sequence of Lymnaea stagnalis depicted in SEQ ID No. 2 counted from the first amino acid of the signal peptide; the letter before the number indicates the original amino acid and the letter after the number indicates the mutant amino acid) N85D, H164Y, D194N, Y204P, Y211P and D213N.

Thus the invention pertains to water-soluble proteins derived from molluscan, preferably acetylcholine binding proteins (AChBP's), which are capable of forming multimers, and are capable of binding a ligand of a ligand-gated receptor. These proteins comprise, on the one hand, at least of the amino acids of the AChBP determining solubility of the AChBP in the same positions as in the AChBP, and, on

10

WO 01/58951 PCT/EP01/01457

-8

the other hand, amino acids determining binding to the ligand of the ligand-gated receptor. The degree of identity with the molluscan AChBP sequence can be defined by amino acid identity, of at least 15%, preferably 20%, more preferably 30%, still more preferably 40%, preferably at least 50 or even at least 60%, preferably more than 70%, more preferably more than 80% and most preferably at least 90% identity, or more, as determined, e.g., using the art-known BLAST algorithm. The amino acids determining binding to the ligand should comprise at least 4 amino acids, preferably at least 6 or even at least 8 amino acids, including a series of at least 3 or 4 amino acids, corresponding to the receptor sequence and preferably differing from the corresponding AChBP amino acids. Preferred embodiments of these proteins are further defined below. Usually, the water-soluble ligand-binding protein or domain as part of a for example chimeric ligand-gated ion channel will comprise 200-240 amino acids. The ligand is preferably acetylcholine, nicotine, lophotoxin, d-tubocurarine, carbamylcholine, galanthamine or epibatidine.

Said ligand-gated receptor can be derived from an arthropod (preferably insect), a plant (preferably a higher plant, most preferably a seed plant) or a chordate (preferably a mammalian, most preferably human), preferably said ligand-gated receptor is a nicotinic acetylcholine receptor.

Usually, the said amino acids in the water-soluble ligand-binding proteins of the invention, which determine solubility are in the same positions as in the AChBP having the amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4, 6 or 8. The solubility determining regions are based on solvent accessibility in structure. The respective amino acid residues can be chosen for example according to Figure 10 or 11 in which the solvent accessible regions are indicated. Preferably, the water-soluble ligand-binding protein of the invention comprises an amino acid sequence having at least 40% amino acid identity to the amino acid sequence of the mature AChBP comprising the amino acid sequence of any one of SEQ ID Nos. 2, 4, 6 or 8, in which the ligand binding amino acids have been replaced with the corresponding amino acids of a ligand-gated receptor.

In one embodiment of the protein of the invention said solubility-determining amino acids (a) comprise hydrophilic amino acids (Asp, Glu, Arg, Lys) from the sequences 20-44, 73-81, 86-92, 112-120, 135-152, 166-189, 196-20, 209-213, and/or 219-227 of SEQ ID No. 2.

The amino acid sequences of L-AChBP_T1 (SEQ ID No. 2) and T2 (SEQ ID No. 4) are almost similar. For the sake of clarity, reference is always made to L-AChBP_T1 (SEQ ID No. 2). However, all references to amino acid residues within are valid for

both T1 and T2, with the noticeable exceptions of Arg(167) becoming Gly(167) and and Thr(203) becoming Ile(203). Furthermore, regarding the amino acid residues (domains) from L-AChBP_T1 and the corresponding residues from B-AChBP the following list provide those amino acid positions in which L-AChBP and B-AChBP differ. All amino acid residue numbers below correspond to their position within the amino acid sequence of the immature protein (numbering starting at methionine (1). One could also start numbering at the start of the amino acid sequence of the mature sequence (L(1)DRAD for L-AChBP and Q(1)IRW for B-AChBP). When using this second method (1st amino acid of the mature seq. = position 1) simply subtract 19 from the L-AChBP position numbers and 21 from the B-AChBP position numbers, for example Asp(36) becomes Asp(17) for L-AChBP) and Asp(15) for B-AChBP. For the further embodiments the positions are given for L-AChBP T1 (SEQ ID No. 2) followed by an indication of the corresponding amino acid positions in the amino acid sequence of L-AChBP_T2 (SEQ ID No. 4) and B-AChBP_T1 (SEQ ID No. 6) & B-AChBP T2 (SEQ ID No. 8) in the form of (L-AChBP_T1&T2 : B-AChBP_T1&T2).

In a preferred embodiment said solubility determining amino acids (a) comprise amino acids Asp(36), Asp(68), Glu(115), Arg(137), Asp(143), Asp(148), Glu(150), Arg(167), Arg(189), Glu(215) of SEQ ID No.2, wherein Asp may be exchanged for Glu and vice versa and Lys may be exchanged for Arg and vice versa (L-AChBP_T1&T2: B-AChBP_T1&T2; Asp(36): Asp(36); Asp(68): Asp(68); Glu(115): Glu(116); Arg(137): Arg(138); Asp(143): Asp(144); Asp(148): Asp(149); Glu(150): Glu(151); Arg(167): Gly(167), in L-AChBP_T2: Lys(168); Arg(189): Lys(190); Glu(215): Glu(216).

25

30

35

5

10

15

20

In a still more preferred embodiment the water-soluble ligand-binding protein comprises the amino acids Cys(142), Thr(149), Ala(153), Thr(154), Cys(155), Arg(156), Ile(157) and/or Lys(158) of SEQ ID No. 2. (L-AChBP_T1&T2: B-AChBP_T1&T2; Cys(142): Cys(143); Thr(149): Thr(150); Ala(153): Ala(154); Thr(154): Thr(155); Cys(155): Cys(156); Arg(156): Arg(157); Ile(157): Ile(158); Lys(158): Lys(159). In a further embodiment the water-soluble ligand-binding protein comprises either in addition or alternatively the amino acids (b) Pro(39), Trp(77), Trp(101), Pro(103), Asp(194), and/or Ser(161) of SEQ ID No. 2 (L-AChBP_T1&T2: B-AChBP_T1&T2; Pro(39): Pro(39); Trp(77): Trp(77); Trp(101): Trp(102); Pro(103): Pro(104); Ser(161): Ser(162); Asp(194): Ser(195).

In a still further embodiment the water-soluble ligand-binding protein comprises either

10

15

30

35

WO 01/58951 PCT/EP01/01457

-10

in addition or alternatively to the above described embodiments amino acid sequences 165-169 and/or 200-203 of SEQ ID No. 2 have been exchanged with the corresponding sequence of the ligand-gated receptor (L-AChBP_T1&T2: B-AChBP_T1&T2; His(165)-Iso(169):. Asp(166)-Phe(170) (B-AChBP_T1): Asp(166)-Leu(170) (B-AChBP_T2); Asn(200)-Thr(203); Iso(203) for L-AChBP_T2: Asn(201)-Lys(204).

The amino acids determining binding to the ligand of the nicotinic acetylcholine receptor include three stretches on the nAChR alpha subunits. These stretches contain amino acids that are conserved throughout the various nAChR alpha subunits and that are essential for ligand binding. These stretches (corresponding to the Torpedo alpha subunit) are (numbering of nAChR α 7 as depicted in SEQ ID No. 9): Trp (108) - Tyr (115), Trp (108) and Tyr (115) being essential; Trp (171) - Tyr (173), the amino acids Trp (171) and Tyr (173) being essential; Tyr (210) - Tyr (217), the amino acids Tyr (210), Cys (212), Cys (213) and Tyr (217) being essential. In the chimeric proteins according to the invention, at least the essential amino acids of at least one of these stretches haven been substituted for the corresponding amino acids. Preferably, the entire stretches have been substituted.

In a particularly preferred embodiment of the invention, the water-soluble ligand-binding protein is capable of binding a ligand of an acetylcholine receptor, wherein in said protein at least one of the amino acid sequences Trp(101) - Tyr(T108), Trp(162) - His(164) and Tyr(204) - Tyr(211) of SEQ ID No. 2 has been exchanged with the corresponding sequence of the acetylcholine receptor (L-AChBP_T1&T2 : B-AChBP_T1&T2; Trp(101)-Tyr(108): Trp(102)-Tyr(109); Trp(162)-His(164): Trp(163)-His(165), (B-AChBP_T1) : Trp(163)-Phe(165) (B-AChBP_T2); Tyr(204)-Tyr(211): Tyr(205)-Tyr(212).

On the basis of homology to the AChBPs, it is possible to change amino acid residues in the original amino acid sequence of the ligand-gated ion channel, which are not critical to ligand-binding or essential for the tertiary and quaternary structure of the receptor but could be substituted to amino acid residues which according to the AChBP in particular the crystal structure contributes to their water-solubility. As a result the ligand-gated ion channel or its ligand-binding domain or the respective monomers and pentamers are for example expected to be more easily expressible in recombinant expression system and more importantly amenable to crystallization, allowing the construction of three-dimensional models of their ligand binding domains.

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-11

Thus, in another embodiment the present invention relates to a method for the production of a water-soluble ligand-gated receptor or a corresponding ligand-binding domain or for improving the water solubility and accessibility to crystallization of such a receptor or domain, said method comprising altering the amino acid sequence of the extracellular domain of a ligand-gated receptor by way of substituting, adding, deleting or modifying at least one amino acid at a position corresponding to an amino acid determining or contributing to the water-solubility of the above-described watersoluble ligand-binding protein of the present invention The method of the invention can be performed using conventional techniques known in the art, for example, by using amino acid deletion(s), insertion(s), substitution(s), addition(s), and/or recombination(s) and/or any other modification(s) known in the art either alone or in combination. Methods for introducing such modifications in the DNA sequence underlying the amino acid sequence of the ligand-binding domain a ligand-gated ion channel are well known to the person skilled in the art; see, e.g., Sambrook, Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory (1989) N.Y. The resulting ligand-gated receptor or ligand-binding domain retains comparable in vitro and preferably also in vivo ligand-binding activity to that of the ligand-gated ion channel, and more importantly, allow complete crystallization of the protein such that they may be characterized by X-ray crystallography. The X-ray crystallographic data can be used for example for identification and construction of possible therapeutic compounds in the treatment of various disease conditions.

As has been discussed herein before, the ligand-gated ion channel superfamily including nACh, 5-HT3, glycine, GABA_A, and GABA_C receptors as well as invertebrate glutamate ion-channels and MOD-1 serotonin channel contain extracellular ligand binding domains that are homologous to the AChBP. Many of these receptors are promising drug targets. Therefore, the ligand-gated receptor to be modified is preferably one of those of the mentioned superfamily, most preferably it is nAChR.

Information on the nucleotide and amino acid sequences, structural elements, functional assays of the nAch, 5-HT3, glycine, GABA_A, and GABA_C receptors can be found in the prior art. For example, the nicotinic receptors at the amino acid level are described in Corringer et al., Annu. Rev. Pharmacol. Toxicol. 40 (2000), 431-458. Means for retrieving nucleotide and amino acid sequences, performing sequence alignments in order to identify the most likely critical amino acid residues are described below and in the examples; for further general information see the review on periplasmic binding protein (PBP), an ancient protein module present in multiple drug receptors by Felder et al., PharmSci. 1(2) (1999).

In a preferred embodiment of the method of the present invention, said at least one amino acid is altered to the corresponding amino acid of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8, or to a an equivalent amino acid, preferably in which said solubility-determining amino acids comprise solvent accessible regions in the crystal structure according to Figure 10 or 11. Preferred amino acid sequence positions and amino acid substitutions are described above for the AChBP and can be applied generally in the method of the present invention.

It is expected that the insertion of the loop Cys123-Cys136 of the mature AChBP SEQ ID No. 2 into the equivalent region (Cys127-Cys141) in the mature nicotinic $\alpha 7$ homopentamer ligand binding domain creates an easily expressed form of this protein. Likewise, this loop or an equivalent loop from other water-soluble ligand proteins of the present invention can be inserted into the equivalent region of other homopentameric ligand binding domains of ligand gated ion channels such as the glycine receptor and the 5-HT3 receptor to create an easily expressed form of those proteins.

Thus, in one embodiment, the present invention relates to any one of the above described methods, wherein loop Cys123-Cys136 of SEQ ID No. 2 is inserted into the corresponding region of the ligand binding domain of the ligand-gated receptor.

20

25

35

10

15

The above described water-soluble ligand-gated receptor or a corresponding ligand-binding domain are usually prepared by site-directed mutagenesis of the underlying encoding polynucleotide. Once the corresponding polynucleotide has been generated it can be used to express the altered ligand-gated receptor or a corresponding ligand-binding domain. Thus, the method of the present invention commonly comprises

- (a) culturing a host cell transfected with and capable of expressing a
 polynucleotide comprising a nucleotide sequence encoding the altered
 amino acid sequence; and optionally
- 30 (b) recovering said water-soluble ligand-gated receptor or corresponding ligand-binding domain from the culture.

Methods for the expression and purification of the water-soluble ligand-gated receptor or corresponding ligand-binding domain of the present invention are described further below. Preferably, the expression system described in Examples 4 and 5, or corresponding expression systems are used.

PCT/EP01/01457

WO 01/58951

5

10

15

. 20

25

30

35

-13

The present invention also relates to the a water-soluble ligand-gated receptor and ligand-binding domain obtainable by the above described methods of the invention. Preferably, said water-soluble ligand-gated receptor exhibits a 10-fold, more preferably 100-fold, still more preferably 1000-fold and most preferably 10000-fold higher solubility in water than the corresponding wild type, preferably human ligand-gated receptor. However, improvements in water solubility of about 2 to 5 fold is also already advantageous. The average hydrophobicity may be in the range of –100 to – 400. Accordingly, the present invention provides methods for the prediction and creation of mutants and chimeras of ligand binding domains of homopentameric acetylcholine receptor subtypes and of other homopentameric ion channels with increased solubility.

In one embodiment the water-soluble ligand-binding protein of the invention further comprises a spacer sequence allowing coupling with a carrier body. The spacer sequence may be an amino acid sequence encodable by a polynucleotide or other molecule such as polymethylene anchor groups commonly used in chip technology. The chimeric protein of the invention may further comprise a spacer sequence, which allows coupling of the protein to a carrier body. Such spacer sequence may be e.g. an oligo-histidine stretch attached to the C-terminus of the protein. Such an oligohistidine stretch is capable of binding to Talon@ metal affinity beads or similar carriers. Such binding stretches have no detectable influence on the pharmacological properties of the proteins. The chimeric proteins according to the invention can be used for screening of specific binding of potential drugs, in particular screening for modulators of ion-channel opening. Conventional in vitro screening techniques, such as phage display technology, can be used for this purpose. High-throughput assays, possibly in combination with combinatorial chemistry can also be used. Specific binding of test compounds to the (immobilised) chimeric proteins of the invention can be performed e.g. by competition binding assays using alpha bungarotoxin as a competitor. The invention also concerns test kits containing the proteins described above, together with further means for carrying out a screening test, such as carriers, labels, diluents, other chemicals etc.

In addition, the present invention relates to fusion proteins comprising the watersoluble ligand-binding protein of the invention or a binding fragment thereof and a fragment of a ligand-gated receptor. The term "fusion protein" as used herein refers to protein constructs that are the result of combining multiple protein domains or linker regions for the purpose of gaining the combined functions of the domains or

-14

linker regions. This is may be accomplished by molecular cloning of the nucleotide sequences encoding such domains to produce a new polynucleotide sequence that encodes the desired fusion protein. Alternatively, creation of a fusion protein may be accomplished by chemically joining two proteins. A fusion protein of the present invention preferably comprises at least the ligand-binding domain of the AChBP or of a ligand-gated ion channel, which has been modified in accordance with the above described methods.

Nicotinic acetylcholine receptors are comprised of five subunits, selected from a related family of subunit proteins. The neuronal subunits fall into two main types depending on the presence or absence of a pair of vicinal cysteines close to the binding site for acetylcholine. Thus all α-subunits contain paired cysteine residues thought to play a role in binding of nicotinic agonists (Aplin and Wonnacott, 48 (1994), 473-477), whereas the β -subunits do not. There are ten known alpha subunits, $\alpha 1$ to α10, and at least four beta subunits, β1 to β4. Receptors comprise at least one alpha subunit which in some cell types combine with a beta subunit and in some cases a gamma, delta and epsilon subunit. For example, the AChR at the neuromuscular junction is believed to have an (α1)2β1γδ stoichiometry. Within the group of αsubunits there is marked diversity in the manner in which a complete functional nAChR is formed. The majority of the α subunits only form functional receptors when combined as a heteropentamer with β-subunits in the CNS (McGehee and Role, Annual Review of Physiology 57 (1995), 521-546). However, α 7, α 8 and α 9 nAChR subunits and the related 5-HT3A subunit are capable of forming functional homopentameric receptors. In this respect it is interesting that the phylogenetic relationship between nAChR subunits suggest that α7, α8, α9 and the related 5-HT3A subunit are more related to each other than to the subunits which only form heteropentameric receptors. Sequence homologies indicate that the α 7, α 8 and α 9 subunits form a distinct subgroup of the alpha subunits.

As is evident form the foregoing, the above described water-soluble ligand-binding protein or receptor or ligand-binding domain thereof can be used for forming complexes of homo- or heteromultimers, such as a dimer, pentamer or decamer consisting of at least one monomer of the mentioned proteins of the present invention. Preferably, these multimers constitute a function ligand-gated receptor. Preferably, said ligand-gated receptor is related to the nAchR.

35

10

15

20

25

30

The present invention also relates to the production of synthetic heteropentamers resembling heteropentameric gated ion-channels by mutation of AChBP, using

PCT/EP01/01457

WO 01/58951

-15

knowledge of the crystal structure about the primary and secondary contact regions; see infra. Preferably, said synthetic heteropentamer's resembles a heteropentameric nicotinic acetylcholine receptor. Accordingly, the present invention more generally relates to a ligand-gated ion channel comprising any one of the above described water-soluble ligand-binding proteins or receptors of the invention as a monomer, homo- or heterodimer or -pentamer. This method therefore allows the prediction and creation of mutants and chimeras of nicotinic acetylcholine receptors and other ligand-gated ion channels that are insensitive or more sensitive to toxin binding, e.g. bungarotoxin, lophotoxin, conotoxin, and other toxins that inhibit ligand-gated ion channels. Preferably, said ligand-gated ion channel is less or more sensitive to binding of toxins such as bungarotoxin, lophotoxin or conotoxin compared to the wild type ligand-gated ion channel.

Further information and examples how to create chimeric ligand-binding proteins in accordance with the present invention is given in Example 10.

15

20

25

30

35

10

5

The nucleotide and amino acid sequences of the acetylcholine, 5-HT3, glycine, GABA_A, and GABA_C receptors can be easily retrieved from public database, for example from the internet using http://www.ncbi.nlm.nih.gov/Entrez. The citations also include a reference to the corresponding publication also reporting on the functional expression of the respective receptor.

The use of recombinant acetylcholine-gated ion channels and functionally assays in the discovery of putative novel ligands has been described in Cosford, Pharm. Acta Helv. (2000), 74(2-3), 125-130. Furthermore, the cell-free expression and functional reconstitution of homo-oligomeric α7 nicotinic acetylcholine receptors into planar lipid bilayers has been reported by Lyford and Rosenberg, J. Biol. Chem. (1999), 274(36), 25675-25681. The use of functional assays of cloned and native muscarinic acetylcholine receptors for determining the selectivity profile of toxins has been described by Olianas et al. (J. Pharmacol. Exp. Ther. 288 (1999), 164-170). A system for the evaluation of pharmacological differences and similarities between 5-HT3 receptors stably transfected cells is provided by for example Bruss et al., Naunyn-Schmiedebergs Archives of Pharmacology 360 (1999), 225-33. The primary structure and functional expression of the 5-HT3 receptor is described in Maricq et al., Science 254 (1991), 432-437. Likewise, the stable expression of human glycine α 1 and α 2 receptor monomers in mouse L(tk-) cells and their use for the study of the physiology and pharmacology of functional glycine receptors is described in Wick et al., J. Neurosci. Methods 87 (1999), 97-103. An example for the measurement of the

-16

pharmacology of recombinant GABA_A receptor subtypes is described in Simpson et al., J. Neurosci. Methods 99 (2000), 91-100. Further examples for assay systems are given below.

The described methods as well as others known to the person skilled in the art can be used for example to

- (1) express and characterise the water-soluble ligand-binding proteins and ligandgated ion channels of the present invention; and
- (2) use stably transfected cells expressing the above described ligand-gated ion channels for the identification of novel ligands.

10

15

20

25

30

35

5

The present invention also relates to polynucleotides encoding the water-soluble ligand-binding proteins and ligand-gated ion channels of the present invention, and multimers thereof, preferably dimers or pentamers. Such polynucleotide may be a DNA such as a cDNA, or an RNA such as mRNA or any other form of nucleic acid including synthetic or modified derivatives and may encode the polypeptide in a continuous sequence or in a number of sequences interrupted by intervening sequences. In which ever form it is present, the polynucleotide is an isolated polynucleotide in that it is removed from its naturally-occurring state. This aspect of the invention is based on the cloning of the cDNA for ligand-binding proteins. In a preferred embodiment, the polynucleotide comprises the nucleotide sequence of any one of SEQ ID Nos. 1, 3, 5 or 7, optionally including one or more mutations or deletions which do not substantially affect the activity of the polypeptide encoded thereby. Such mutations include those arising from the degeneracy of the genetic code, as well as those giving rise to any of the amino acid mutations or deletions discussed above. The polynucleotides of the invention preferably comprise

- (a) a nucleotide sequence having at least 15 continuous nucleotides of the nucleotide sequence depicted in any one of SEQ ID Nos. 1, 3, 5 or 7 or a degenerated nucleotide sequence thereof; or
- (b) a nucleotide sequence capable of hybridizing to a nucleotide sequence of (a) under stringent hybridisation conditions.

Typically, selective hybridization will occur when there is at least about 55% sequence identity -- preferably at least about 65%, more preferably at least about 75%, and most preferably at least about 90% -- over a stretch of at least about 14 nucleotides; see, e.g., Kanehisa, Nucleic Acids Res. 12 (1984), 203-213, herein incorporated by reference. Nucleic acid hybridization will be affected by such conditions as salt concentration, temperature, solvents, the base composition of the

PCT/EP01/01457

5

10

15

25

30

35

hybridizing species, length of the complementary regions, and the number of nucleotide base mismatches between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art.

"Stringent hybridization conditions" and "stringent wash conditions" in the context of nucleic acid hybridization experiments depend upon a number of different physical parameters. The most important parameters include temperature of hybridization, base composition of the nucleic acids, salt concentration and length of the nucleic acid. One having ordinary skill in the art knows how to vary these parameters to achieve a particular stringency of hybridization. In general, "stringent hybridization" is performed at about 25°C below the thermal melting point (T m) for the specific DNA hybrid under a particular set of conditions.

"Stringent washing" is performed at temperatures about 5°C lower than the Tm for the specific DNA hybrid under a particular set of conditions. The Tm is the temperature at which 50% of the target sequence hybridizes to a perfectly matched probe; see Sambrook et al., page 9.51, hereby incorporated by reference. The Tm for a particular DNA-DNA hybrid can be estimated by the formula:

Tm = 81.5°C + 16.6 (log10[Na+]) + 0.41 (fraction G + C) - 0.63 (% formamide) - (600/l) where I is the length of the hybrid in base pairs.

The Tm for a particular RNA-RNA hybrid can be estimated by the formula:

20 Tm = 79.8° C + 18.5 (log10[Na+]) + 0.58 (fraction G + C) + 11.8 (fraction G + C)2 - 0.35 (% formamide) - (820/1).

The Tm for a particular RNA-DNA hybrid can be estimated by the formula:

 $Tm = 79.8^{\circ}C + 18.5(log10[Na+]) + 0.58$ (fraction G + C) + 11.8 (fraction G + C)2 - 0.50 (% formamide) - (820/I).

In general, the Tm decreases by 1-1.5°C for each 1% of mismatch between two nucleic acid sequences. Thus, one having ordinary skill in the art can alter hybridization and/or washing conditions to obtain sequences that have higher or lower degrees of sequence identity to the target nucleic acid. For instance, to obtain hybridizing nucleic acids that contain up to 10% mismatch from the target nucleic acid sequence, 10-15°C would be subtracted from the calculated Tm of a perfectly matched hybrid, and then the hybridization and washing temperatures adjusted accordingly. Probe sequences may also hybridize specifically to duplex DNA under certain conditions to form triplex or other higher order DNA complexes. The preparation of such probes and suitable hybridization conditions are well known in the art. An example of stringent hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or Northern blot or for screening a library is 50%

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-18

formamide/6X SSC at 42°C for at least ten hours. Another example of stringent hybridization conditions is 6X SSC at 68°C for at least ten hours. An example of low stringency hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or northern blot or for screening a library is 6X SSC at 42°C for at least ten hours. Hybridization conditions to identify nucleic acid sequences that are similar but not identical can be identified by experimentally changing the hybridization temperature from 68°C to 42°C while keeping the salt concentration constant (6X SSC), or keeping the hybridization temperature and salt concentration constant (e.g. 42°C and 6X SSC) and varying the formamide concentration from 50% to 0%. Hybridization buffers may also include blocking agents to lower background. These agents are well-known in the art; see Sambrook et al., pages 8.46 and 9.46-9.58, herein incorporated by reference. Wash conditions also can be altered to change stringency conditions. An example of stringent wash conditions is a 0.2x SSC wash at 65°C for 15 minutes (see Sambrook et al., for SSC buffer). Often the high stringency wash is preceded by a low stringency wash to remove excess probe. An exemplary medium stringency wash for duplex DNA of more than 100 base pairs is 1x SSC at 45°C for 15 minutes. An exemplary low stringency wash for such a duplex is 4x SSC at 40°C for 15 minutes. In general, signal-to-noise ratio of 2x or higher than that observed for an unrelated probe in the particular hybridization assay indicates detection of a specific hybridization.

By the provision of the nucleotide sequences of SEQ ID Nos. 1, 3, 5 and 7 as well as those encoding the amino acid sequences depicted in SEQ ID Nos. 2, 4, 6 and 8 it is possible to isolate identical or similar nucleic acid molecules which encode water-soluble ligand-binding proteins from other species or organisms, in particular orthologous water-soluble ligand-binding protein encoding genes from mammals. The term "orthologous" as used herein means homologous sequences in different species that arose from a common ancestor gene during speciation. Orthologous genes may or may not be responsible for a similar function; see, e.g., the glossary of the "Trends Guide to Bioinformatics", Trends Supplement 1998, Elsevier Science.

In a further aspect, the present invention provides a recombinant polynucleotide comprising a vector incorporating the polynucleotide of the present invention. Many suitable vectors are known to those skilled in molecular biology, the choice of which would depend on the function desired and include plasmids, cosmids, viruses, bacteriophages and other vectors used conventionally in genetic engineering. Methods which are well known to those skilled in the art can be used to construct

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-19

various plasmids and vectors; see, for example, the techniques described in Sambrook, Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory (1989) N.Y. and Ausubel, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. (1989), (1994). Alternatively, the polynucleotides and vectors of the invention can be reconstituted into liposomes for delivery to target cells. As discussed in further details below, a cloning vector was used to isolate individual sequences of DNA. Relevant sequences can be transferred into expression vectors where expression of a particular polypeptide is required. Typical cloning vectors include pBscpt sk, pGEM, pUC9, pBR322 and pGBT9. Typical expression vectors include pTRE, pCAL-n-EK, pESP-1, pOP13CAT, pET, pGEX, pMALC, pPIC9, pBac.

Hence, in a preferred embodiment of the present invention the above-described polyncucleotides either alone or present in a vector are linked to control sequences which allow the expression of the polynucleotide in prokaryotic and/or eukaryotic cells.

The term "control sequence" refers to regulatory DNA sequences which are necessary to effect the expression of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism. In prokaryotes, control sequences generally include promotor, ribosomal binding site, and terminators. In eukaryotes generally control sequences include promotors, terminators and, in some instances, enhancers, transactivators or transcription factors. The term "control sequence" is intended to include, at a minimum, all components the presence of which are necessary for expression, and may also include additional advantageous components.

The term "operably linked" refers to a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences. In case the control sequence is a promotor, it is obvious for a skilled person that double-stranded nucleic acid is preferably used.

Thus, the vector of the invention is preferably an expression vector. An "expression vector" is a construct that can be used to transform a selected host cell and provides for expression of a coding sequence in the selected host. Expression vectors can for instance be cloning vectors, binary vectors or integrating vectors. Expression comprises transcription of the nucleic acid molecule preferably into a translatable mRNA. Regulatory elements ensuring expression in prokaryotic and/or eukaryotic

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-20

cells are well known to those skilled in the art. In the case of eukaryotic cells they comprise normally promotors ensuring initiation of transcription and optionally poly-A signals ensuring termination of transcription and stabilization of the transcript. Possible regulatory elements permitting expression in prokaryotic host cells comprise, e.g., the PL, lac, trp, T7 or tac promotor in E. coli, and examples of regulatory elements permitting expression in eukaryotic host cells are the AOX1 or GAL1 promotor in yeast or the CMV-, SV40-, RSV-promotor (Rous sarcoma virus), CMV-enhancer, SV40-enhancer or a globin intron in mammalian and other animal cells. In this context, suitable expression vectors are known in the art such as Okayama-Berg cDNA expression vector pcDV1 (Pharmacia), pCDM8, pRc/CMV, pcDNA1, pcDNA3 (In-vitrogene), pSPORT1 (GIBCO BRL). An alternative expression system which could be used to express the protein is an insect system. In one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in Spodoptera frugiperda cells or in Trichoplusia larvae. The coding sequence of a nucleic acid molecule of the invention may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promotor. Successful insertion of said coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect S. frugiperda cells or Trichoplusia larvae in which the protein of the invention is expressed (Smith, J. Virol. 46 (1983), 584; Engelhard, Proc. Nat. Acad. Sci. USA 91 (1994), 3224-3227).

In plants, promotors commonly used are the polyubiquitin promotor, and the actin promotor for ubiquitous expression. The termination signals usually employed are from the Nopaline Synthase promotor or from the CAMV 35S promotor. A plant translational enhancer often used is the TMV omega sequences, the inclusion of an intron (Intron-1 from the Shrunken gene of maize, for example) has been shown to increase expression levels by up to 100-fold. (Mait, Transgenic Research 6 (1997), 143-156; Ni, Plant Journal 7 (1995), 661-676). Additional regulatory elements may include transcriptional as well as translational enhancers. Advantageously, the above-described vectors of the invention comprises a selectable and/or scorable marker. Selectable marker genes useful for the selection of transformed cells and, e.g., plant tissue and plants are well known to those skilled in the art and comprise, for example, antimetabolite resistance as the basis of selection for dhfr, which confers resistance to methotrexate (Reiss, Plant Physiol. (Life Sci. Adv.) 13 (1994), 143-149); npt, which confers resistance to the aminoglycosides neomycin.

20

25

30

35

WO 01/58951 PCT/EP01/01457

-21

kanamycin and paromycin (Herrera-Estrella, EMBO J. 2 (1983), 987-995) and hygro, which confers resistance to hygromycin (Marsh, Gene 32 (1984), 481-485).

Useful scorable markers are also known to those skilled in the art and are commercially available. Advantageously, said marker is a gene encoding luciferase (Giacomin, Pl. Sci. 116 (1996), 59-72; Scikantha, J. Bact. 178 (1996), 121), green fluorescent protein (Gerdes, FEBS Lett. 389 (1996), 44-47) or β-glucuronidase (Jefferson, EMBO J. 6 (1987), 3901-3907). This embodiment is particularly useful for simple and rapid screening of cells, tissues and organisms containing a vector of the invention.

The proteins can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, size exclusion chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") or FPLC is employed for purification.

The present invention furthermore relates to host cells produced by introducing a nucleic acid molecule into the host cell which upon its presence in the cell mediates the expression of a gene encoding water-soluble ligand-binding proteins or comprising a polynucleotide or a vector as described above or a polynucleotide according to the invention wherein the polynucleotides and/or nucleic acid molecule is foreign to the host cell. By "foreign" it is meant that the polynucleotide or nucleic acid molecule is either heterologous with respect to the host cell, this means derived from a cell or organism with a different genomic background, or is homologous with respect to the host cell but located in a different genomic environment than the naturally occurring counterpart of said nucleic acid molecule. This means that, if the nucleic acid molecule is homologous with respect to the host cell, it is not located in its natural location in the genome of said host cell, in particular it is surrounded by different genes. In this case the polynucleotide may be either under the control of its own promotor or under the control of a heterologous promotor. The vector or nucleic acid molecule according to the invention which is present in the host cell may either be integrated into the genome of the host cell or it may be maintained in some form extrachromosomally. In this respect, it is also to be understood that the nucleic acid molecule of the invention can be used to restore or create a mutant gene via homologous recombination.

15

20

25

30

WO 01/58951 PCT/EP01/01457

-22

The host cell can be any prokaryotic or eukaryotic cell, such as bacterial, insect, fungal, plant or animal cells.

The term "prokaryotic" is meant to include all bacteria which can be transformed or transfected with a DNA or RNA molecules for the expression of a protein of the invention. Prokaryotic hosts may include gram negative as well as gram positive bacteria such as, for example, E. coli, S. typhimurium, Serratia marcescens and Bacillus subtilis. The term "eukaryotic" is meant to include yeast, higher plant, insect and preferably mammalian cells. Depending upon the host employed in a recombinant production procedure, the protein encoded by the polynucleotide of the present invention may be glycosylated or may be non-glycosylated. The water-soluble ligand-binding protein of the invention may or may not also include an initial methionine amino acid residue. A polynucleotide of the invention can be used to transform or transfect the host using any of the techniques commonly known to those of ordinary skill in the art. Furthermore, methods for preparing fused, operably linked genes and expressing them in, e.g., mammalian cells and bacteria are well-known in the art (Sambrook, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1989).

Thus the present invention provides a cell capable of expressing a polypeptide as discussed herein. The cell comprises a recombinant host cell usually incorporating the polynucleotide. Preferably, the host cell incorporates the polynucleotide as the recombinant polynucleotide. Any suitable host cell may be chosen, again depending on the intended purpose. Suitable host cells include XLI-BLUE, B21(DE3)pLysS, HB101, SOLR and SP-Q01 (Saccharomyces pombe).

Using an appropriate combination of host cell, vector and polynucleotide, an expression system can be provided so as to obtain a polypeptide useful in the present invention. This may comprise a fusion polypeptide encoded by the recombinant polynucleotide, a part of which is encoded by the vector. Typically, the vector will have a promotor region, which is usually inducible, leading to 5' coding region associated with the promotor. By appropriate manipulation, the polynucleotide encoding the polypeptide can be attached to the 5' coding region in frame. In this way, expression of the nucleotide sequence downstream of the promotor region gives rise to the fusion polypeptide which includes the polypeptide of the present invention.

The present invention also relates to an antigen comprising an epitope of at least 5 continuous amino acids of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8 and/or said epitope is detectable by a monoclonal or polyclonal

PCT/EP01/01457

WO 01/58951

5

10

15

20

25

30

35

-23

antibody which recognises, preferably with a binding affinity of at least 10.7M, a protein of the invention as described above. In the present invention, "epitopes" refers to fragments of the AChBP of the invention having antigenic or immunogenic activity in an animal. A preferred embodiment of the present invention relates to antigens comprising an epitope, as well as the polynucleotide encoding this fragment. A region of a protein molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response; see, for instance, Geysen, Proc. Natl. Acad. Sci. USA 81 (1983); 3998-4002. Fragments which function as epitopes may be produced by any conventional means; see, e.g., Houghten, Proc. Natl. Acad. Sci. USA 82 (1985), 5131-5135 further described in U.S. Patent No. 4,631,211. In the present invention, antigenic epitopes preferably contain a sequence of at least five, six, seven, more preferably at least nine, and most preferably between about 15 to about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope; see, for instance, Wilson, Cell 37 (1984), 767-778; Sutcliffe, Science 219 (1983), 660-666). Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art; see, for instance, Sutcliffe, supra; Wilson, supra; Chow, Proc. Natl. Acad. Sci. USA 82 (1985), 910-914; and Bittle, J. Gen. Virol. 66 (1985); 2347-2354. A preferred immunogenic epitope includes the soluble protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting.)

The present invention also relates to antibodies specifically recognizing the water-soluble ligand-binding protein and ligand-gated ion channels of the present invention, in particular recognizing the above described antigen or epitope. As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules as well as antibody fragments (such as, for example, Fab and F(ab')₂ fragments) which are capable of specifically binding to protein. Fab and F(ab')₂ fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody; see, e.g., Wahl, J. Nucl. Med. 24 (1983), 316-325. Thus, these fragments are preferred, as well as the products of a FAB or other immunoglobulin expression

10

15

20

25

30

35

PCT/EP01/01457

-24

library. Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies; see also infra. Said antibody can be a monoclonal antibody, a polyclonal antibody, a single chain antibody, human or humanized antibody, primatized, chimerized or fragment thereof that specifically binds said peptide or polypeptide also including bispecific antibody, synthetic antibody, antibody fragment, such as Fab, Fv or scFv fragments etc., or a chemically modified derivative of any of these. The general methodology for producing antibodies is well-known and has been described in, for example, Köhler and Milstein, Nature 256 (1975), 494 and reviewed in J.G.R. Hurrel, ed., "Monoclonal Hybridoma Antibodies: Techniques and Applications", CRC Press Inc., Boco Raron, FL (1982), as well as that taught by L. T. Mimms et al., Virology 176 (1990), 604-619. Furthermore, antibodies or fragments thereof to the aforementioned peptides can be obtained by using methods which are described, e.g., in Harlow and Lane "Antibodies, A Laboratory Manual", CSH Press, Cold Spring Harbor, 1988. For the production of antibodies in experimental animals, various hosts including goats, rabbits, rats, mice, and others, may be immunized by injection with polypeptides of the present invention or any fragment or oligopeptide or derivative thereof which has immunogenic properties. Techniques for producing and processing polyclonal antibodies are known in the art and are described in, among others, Mayer and Walker, eds., "Immunochemical Methods in Cell and Molecular Biology", Academic Press, London (1987). Polyclonal antibodies also may be obtained from an animal, preferably a mammal, previously infected with the virus of the invention. Methods for purifying antibodies are known in the art and comprise, for example, immunoaffinity chromatography. Depending on the host species, various adjuvants or immunological carriers may be used to increase immunological responses. Such adjuvants include, but are not limited to, Freund's, complete or incomplete adjuvants, mineral gels such as aluminium hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions and dinitrophenol. An example of a carrier, to which, for instance, a peptide of the invention may be coupled, is keyhole limpet hemocyanin (KLH). When derivatives of said antibodies are obtained by the phage display technique, surface plasmon resonance as employed in the BIAcore system can be used to increase the efficiency of phage antibodies which bind to an epitope of the peptide or polypeptide of the invention (Schier, Human Antibodies Hybridomas 7 (1996), 97-105; Malmborg, J. Immunol. Methods 183 (1995), 7-13). In many cases, the binding phenomena of antibodies to antigens is equivalent to other ligand/anti-ligand binding.

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-25

In another embodiment the present invention relates to an oligonucleotide probe comprising a nucleotide sequence having at least 15 continuous nucleotides of a polynucleotide of the invention and/or encoding the above described antigen. Such oligonucleotides will usually specifically hybridize to a polynucleotide encoding a water-soluble ligand-binding protein of the Invention. Specific hybridization occurs preferably under stringent conditions and implies no or very little cross-hybridization with nucleotide sequences encoding no or substantially different proteins. Such nucleic acid molecules may be used as probes and/or for the control of gene expression. Nucleic acid probe technology is well known to those skilled in the art who will readily appreciate that such probes may vary in length. Preferred are nucleic acid probes of 17 to 35 nucleotides in length. Of course, it may also be appropriate to use nucleic acids of up to 100 and more nucleotides in length. The nucleic acid probes of the invention are useful for various applications. On the one hand, they may be used as PCR primers for amplification of polynucleotides according to the invention. Another application is the use as a hybridization probe to identify polynucleotides hybridizing to the polynucleotides of the invention by homology screening of genomic DNA libraries. Nucleic acid molecules according to this preferred embodiment of the invention which are complementary to a polynucleotide as described above may also be used for repression of expression of a gene comprising such a polynucleotide, for example due to an antisense or triple helix effect or for the construction of appropriate ribozymes (see, e.g., EP-B1 0 291 533, EP-A1 0 321 201, EP-A2 0 360 257) which specifically cleave the (pre)-mRNA of a gene comprising a polynucleotide of the invention. Selection of appropriate target sites and corresponding ribozymes can be done as described for example in Steinecke, Ribozymes, Methods in Cell Biology 50, Galbraith et al. eds Academic Press, Inc. (1995), 449-460. Standard methods relating to antisense technology have also been described (Melani, Cancer Res. 51 (1991), 2897-2901). Said nucleic acid molecules may be chemically synthesized or transcribed by an appropriate vector containing a chimeric gene which allows for the transcription of said nucleic acid molecule in the cell. Such nucleic acid molecules may further contain ribozyme sequences as described above.

In this respect, it is also to be understood that the polynucleotide of the invention can be used for "gene targeting" and/or "gene replacement", for restoring a mutant gene or for creating a mutant gene via homologous recombination; see for example Mouellic, Proc. Natl. Acad. Sci. USA, 87 (1990), 4712-4716; Joyner, Gene Targeting, A Practical Approach, Oxford University Press.

-26

Furthermore, the person skilled in the art is well aware that it is also possible to label such a nucleic acid probe with an appropriate marker for specific applications, such as for the detection of the presence of a polynucleotide of the invention in a sample derived from an organism, in particular mammals, preferably human. A number of companies such as Pharmacia Biotech (Piscataway NJ), Promega (Madison WI), and US Biochemical Corp (Cleveland OH) supply commercial kits and protocols for these procedures. Suitable reporter molecules or labels include those radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles and the like. Patents teaching the use of such labels include US Patents US-A-3,817,837; US-A-3,850,752; US-A-3,939,350; US-A-3,996,345; US-A-4,227,437; US-A-4,275,149 and US-A-4,366,241. Also, recombinant immunoglobulins may be produced as shown in US-A-4,816,567 incorporated herein by reference.

Furthermore, the so-called "peptide nucleic acid" (PNA) technique can be used for the detection or inhibition of the expression of a polynucleotide of the invention. For example, the binding of PNAs to complementary as well as various single stranded RNA and DNA nucleic acid molecules can be systematically investigated using thermal denaturation and BIAcore surface-interaction techniques (Jensen, Biochemistry 36 (1997), 5072-5077).

20

25

30

35

5

10

15

The present invention also relates to a method for the production of a transgenic non-human animal, preferably transgenic mouse, comprising introduction of a polynucleotide or vector of the invention into a germ cell, an embryonic cell, stem cell or an egg or a cell derived therefrom. The non-human animal can be used in accordance with a screening method of the invention described herein. Production of transgenic embryos and screening of those can be performed, e.g., as described by A. L. Joyner Ed., Gene Targeting, A Practical Approach (1993), Oxford University Press. The DNA of the embryonal membranes of embryos can be analyzed using, e.g., Southern blots with an appropriate probe; see supra. The invention also relates to transgenic non-human animals such as transgenic mouse, rats, hamsters, dogs, monkeys, rabbits, pigs, C. elegans and fish such as Torpedo fish comprising a polynucleotide or vector of the invention or obtained by the method described above, preferably wherein said polynucleotide or vector is stably integrated into the genome of said non-human animal, preferably such that the presence of said polynucleotide or vector leads to the expression of the water-soluble protein of the present invention.

WO 01/58951 PCT/EP01/01457

-27

The present invention further relates to composition comprising any one of the above described water-soluble ligand-binding proteins, multimers such as dimers or pentamers thereof, ligand-gated ion channels, polynucleotides, vectors, host cells, antigens, antibodies, or oligonucleotide probes of the invention; and optionally suitable means for detection or performing a ligand-receptor binding assay. In this context, the present invention also relates to a method for identifying an agonIst/activator or antagonIst/inhibitor of a ligand-gated receptor comprising the steps of:

- (a) contacting the water-soluble ligand-binding protein of the present invention, multimers such as dimers or pentamers thereof, or the ligand-gated ion channel of the invention or a cell expressing said protein in the presence of components capable of providing a detectable signal in response to ligand binding with a compound to be screened under conditions that permit binding of said compound to the ligand-binding protein; and
- 15 (b) detecting the presence or absence of a signal generated from the binding activity of the ligand-binding protein, wherein the presence/increase and absence/decrease of the signal is indicative for an agonist/activator and antagonist/inhibitor, respectively, of a ligand-gated receptor.
- Since ligand-gated receptors are modulated allosterically by natural polyamines, 20 such as spermine, and by polyamine derivatives, such as polyamine amides (e.g. and polymethylene tetraamines (e.g. methoctramine) philanthotoxin-343) (Usherwood, Farmaco. 55 (2000), 202-205) compounds comprising or based on such entities may be used as starting material for screening. An antagonist or agonist that "modulates the activity" of a polypeptide and causes an altered signal, for 25 example response in the cell refers to a compound that alters the activity of the protein so that it behaves differently in the presence of the compound than in the absence of the compound. Typically, the effect of an antagonist is observed as a blocking of agonist-induced receptor activation. Antagonists include competitive as well as non-competitive antagonists. A competitive antagonist (or competitive 30 blocker) interacts with or near the site specific for agonist binding. A non-competitive antagonist or blocker inactivates the function of the receptor by interacting with a site other than the agonist interaction site. As understood by those of skill in the art, bioassay methods for identifying compounds that modulate the activity of receptors such as proteins of the invention generally require comparison to a control. One type 35 of "control" is a cell or culture that is treated substantially the same as the test cell or test culture exposed to the compound, with the distinction that the "control" cell or

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-28

culture is not exposed to the compound. For example, in methods that use voltage clamp electrophysiological procedures, the same cell can be tested in the presence or absence of compound, by merely changing the external solution bathing the cell. Accordingly, the response of the transfected cell to the "control" cell or culture to the same compound under the same reaction conditions. However, "control data" can also be used from the literature.

As described in Example 6 the 3-dimensional structure of AChBP could be solved by X-ray crystallography at 2.7Å resolution (current Rfactor = 27.9 %, Rfree = 30.0 %). In crystals, as in solution, AChBP forms a stable homo-pentamer with dimensions comparable to those of the ligand-binding domain of ligand-gated ion channels, in particular comparable to the nAChR, as determined in EM studies by Unwin and coworkers; see supra. The structural analysis revealed that in the AChBP homopentamer the monomers have immunoglobulin-like topology. At each of five subunit interfaces a ligand-binding site is located, with all residues consistent with biochemical data. In this site a buffer molecule (HERPES) stacks with cation- π interactions on a tryptophan, resembling acetylcholine binding. The AChBP structure is relevant for the development of drugs against, e.g., Alzheimer's disease and nicotine addiction. The high-resolution crystal structure of AChBP, along with biochemical and pharmacological data, supports the teaching of the present invention that the water-soluble ligand-binding proteins of the invention such as AChBP are good mimics of ligand-binding domains of ligand-gated ion channels.

Thus, the present invention relates to a crystal of a water-soluble ligand-binding protein of the invention, preferably in a multimeric form such as dimer, pentamer or decamer. In one embodiment said crystal comprises a protein-ligand complex.

Methods how to employ and analyze such crystals are known to the person skilled in the art; see for example US-A-5,872,011 which describes the crystal structure of a protein-ligand complex containing an N-terminal truncated eIF4E and uses thereof.

The crystal structure of the ligand-gated receptor ligand-binding region in a complex with a ligand, preferably being an antagonist or agonist will reveal the determinants of receptor-antagonist/agonist interactions and how ligand-binding specificity and affinity are altered by remote residues and the redox state of the conserved disulphide bond. The structure may also indicate mechanisms for allosteric effector action and for ligand-induced channel gating. How the information on the crystal structure of a ligand-binding region in a complex with a ligand can be used for the development of agonists and antagonists has been described for the structure of a

10

15

20

25

WO 01/58951 PCT/EP01/01457

-29

glutamate-receptor ligand-binding core in complex with kainate (Armstrong et al., Nature 395 (1998), 913-917).

The crystal of the invention, in particular when comprising nAChR related proteins can be a complex of the protein with a ligand comprising an N-alkylated hydroxyalkyl and/or a quaternary ammonium ion. However, other ligands my be used as well. Preferred ligands comprise 4-(2-Hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), B-bippinatin, lophotoxin, d-tubocurarine, nicotine, acetylcholine, conotoxin, carbamylcholine, galanthamine, epibatidine or alpha-bungarotoxin or derivatives thereof.

Different aspects of X-ray crystallography are such as data collection, structure solution, determining the molecular structure from X-ray diffraction, refinement, etc. are described in the prior art, see, e.g., Powell, Annu. Rep. Prog. Chem., Sect. C: Phys. Chem. 96 (2000), 139-175 and Methods in Enzymology, 276-277, edited by Carter and Sweet, Academic Press, 1997. Current methods and optimization algorithms for the refinement of X-ray crystal structures are described by Van Der Maelen Uria, Crystallogr. Rev. 7 (1999), 125-180.

The crystal of the invention effectively diffracts X-rays for the determination of the atomic coordinates of the protein or protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms. In a preferred embodiment the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 3.0 Angstroms. In a more preferred embodiment the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 2.0 Angstroms. In one embodiment the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of about 2.7 Angstroms.

Preferably, the crystal of the invention is formed by a protein that has an amino acid sequence of amino acids 20 to 223 of SEQ ID No. 2, or an amino acid sequence that differs from amino acid 20 to 223 of SEQ ID No. 2 by only having conservative substitutions. As is described in the examples, the crystals of the AChBP comprise decameric forms of the protein. In order to ease the use of the AChBP protein for analysis and crystallography it is envisaged to create a mutation in residue Asp2 and Asp5 of the mature AChBP SEQ ID No. 2 or 4 to remove the calcium binding site, and prevent creation of a decamer. This deletion can be done for example by

15

20

25

30

WO 01/58951 PCT/EP01/01457

-30

oligonucleotide-directed mutagenesis. Alternatively crystals could be grown in a low calcium concentration or in the absence of calcium.

The crystal of the present invention preferably has (1) a space group of $P2_12_12_1$ and a unit cell of dimensions of a=120.6Å, b=137.0Å and c=161.5Å; (2) a space group of $P4_22_12$ and a unit cell of dimensions of a=b=141.6Å and c=120.8Å or (3) a space group of $P2_1$ and a unit cell of dimensions of a=121.1Å, b=162.1Å, c=139.4Å, β =90.1°.

The crystal of the present invention is preferably from a protein that has secondary structural elements that include .alpha.-helix and antiparallel .beta.-sheets as shown in and described for Figures 7, 10, 11 and/or 12. Most preferably, the crystal of the invention has a three-dimensional structure as defined by atomic coordinates shown in Table 1. Those of skill in the art understand that a set of structure coordinates determined by X-ray crystallography is not without standard error. For the purpose of this invention, any set of structure coordinates for AChBP or AChBP mutants that have a root mean square deviation of protein backbone atoms (N, C.alpha., C and O) of less than 0.75 Angstrom when superimposed - using backbone atoms - on the structure coordinates listed in Table 1 shall be considered identical.

In a most preferred embodiment of the present invention, the crystal has a binding cavity as shown in Figures 6, 8, 9 and/or 13.

In accordance with the findings of the present invention, it is proposed to use the water-soluble ligand-binding proteins of molluscs as the blueprint for the receptor binding site of the ligand-gated ion channel superfamily including nACh, 5-HT3, glycine, GABAA, and GABAC, most preferably for the nAChR. The availability of X-ray structures, and the cloned sequences provide a unique opportunity to understand these receptors at the molecular level, possibly unravel the dynamic changes occurring upon ligand binding, and predict their tertiary and quaternary structure with a higher degree of confidence than possible for other protein modules. This should pave the way for designing ligands selective for any of the multiple subtypes in any of these receptor families. The AChBP-like structures can be used for computerized docking to homology models which leads to the *a priori* discovery of novel ligands before laboratory experiments begin to optimize the drug candidates.

Thus, the present invention also relates to a method of using the crystal of the invention in a drug screening assays, such as comprising:

35 (a) selecting a potential ligand by performing structure assisted drug design with the three-dimensional structure determined for the crystal,

15

20

25

WO 01/58951 PCT/EP01/01457

-31

- wherein said selecting is performed in conjunction with computer modeling; optionally
- (b) contacting the potential ligand with the ligand binding domain of the ligand-gated receptor in an in vitro or in vivo assay; and
- 5 (c) detecting the binding of the potential ligand for the ligand binding domain.

The use of macromolecular crystallography as a tool for investigating drug and receptor interactions, in particular structure-based drug design is reviewed in Oakley and Wilce, Clin. Exp. Pharmacol. Physiol. 27 (2000), 145-151. The desired drug could be an inhibitor or an agonist that mimics endogenous transmitters or ligands. Once the 3-D structure of the relevant target is known, computational processes can be used to search databases of compounds to identify ones that may interact strongly with the target. Lead compounds can be improved using the 3-D structure of the complex of the lead compound and its biological target. The activity of the selected compound can then be tested in a functional assay such as one of those described herein.

Preferably, the potential drug is selected on the basis of its having a greater affinity for the ligand binding domain of the ligand-gated receptor than that of a standard ligand for the ligand binding domain of the ligand-gated receptor. However, the affinity of the selected compound may also be less than that of a standard ligand. Such compounds are useful for example as a lead for the development of further analogues which in turn may have enhanced binding affinity or otherwise beneficial therapeutic properties. On the other hand, the selected compound may bind to a site of the ligand-gated receptor other than known ligands. In a preferred embodiment, the ligand-gated receptor is a nicotinic acetylcholine receptor.

In a further embodiment, the method of the present invention further comprises:

- (d) forming a supplemental crystal of a protein-ligand complex by co-30 crystallization or soaking the crystal of the water-soluble ligand-binding protein with a potential drug, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms, more preferably greater than 3;
- 35 (e) determining the three-dimensional structure of the supplemental crystal;

WO 01/58951 PCT/EP01/01457

-32

- (f) selecting a candidate drug by performing a structure assisted drug design with the three-dimensional structure determined for the supplemental crystal, wherein said selecting is performed in conjunction with computer modeling; optionally
- 5 (g) contacting the candidate drug with a cell that expresses the ligandgated receptor; and
 - (h) detecting a cell response; wherein a candidate drug is identified as a drug when the cell response is altered compared to a cell that has not been contacted with the candidate compound.
- The above described methods can further comprise an initial step that precedes step

 (a) wherein said initial step consists of determining the three-dimensional structure of
 a crystal comprising a protein-ligand complex formed between the water-soluble
 ligand-binding protein, and the ligand of the ligand-gated receptor, wherein the
 crystal effectively diffracts X-rays for the determination of the atomic coordinates of
 the protein-ligand complex to a resolution of greater than 5.0, preferably greater than
 4.0 Angstroms. Preferably, the resolution of crystal diffraction in the above described
 methods is at least 3.0, most preferably at least about 2.7 Angstroms.

In a still further embodiment, the present invention relates to a method of growing a crystal of a protein-ligand complex comprising:

- (a) contacting the water-soluble ligand-binding protein described above with a ligand of a ligand-gated receptor, wherein the water-soluble ligand-binding protein forms a protein-ligand complex with the ligand; and
- (b) growing the crystal of the protein-ligand complex; wherein the

 crystal effectively diffracts X-rays for the determination of the
 atomic coordinates of the protein-ligand complex to a resolution
 of greater than 5.0, preferably greater than 4.0 Angstroms, more preferably at
 least 3.0, most preferably at least about 2.7 Angstroms.
- The crystals of the present invention can also be used in X-ray crystallography—driven screening technique that combines the steps of lead identification, structural assessment, and optimization such as described for example in Nienaber et al., Nature Biotechnol. 18 (2000), 1105 1108. This crystallographic screening method (named CrystaLEAD) has been used to sample large compound libraries and detecting ligands by monitoring changes in the electron density map of the crystal relative to the unbound form. The electron density map yields a high- resolution picture of the ligand–protein complex that provides key information to a structure-

-33

directed drug discovery process. The bound ligand is directly visualized in the electron density map. Ligands that bind away from the targeted site may be ellminated.

The above described methods can be coupled with state-of-the-art laboratory data collection facilities including CCD detectors and data acquisition robotics.

Further embodiments that may be used in accordance with the ligand-binding proteins and receptor of the present invention are described in the prior art, for example ligand screening and design by X-ray crystallography is disclosed in WO99/45379 and WO99/45389; WO00/14105 describes assaying a candidate compound for its ability to interact with a modified receptor tyrosine kinase including obtaining and applying crystallography coordinates to a computer algorithm for generating a model which is applied in an iterative process to various molecular structures in order to identify agonist and antagonists of the receptor. All these methods may be equally applied to the proteins and crystals of the present invention.

15

- 5

10

In one preferred embodiment, the present invention relates to a drug screening assay comprising soaking a crystal of the invention in a solution of compounds to be screened and detecting the binding of the compound to the ligand-binding protein. A possible procedure is also described in Example 9. Besides the detection methods of ligand-binding mentioned above, in the cited documents and in the examples, the detection can also be based on measuring the release of the ligand in the preformed crystal of a protein-ligand complex. As described herein before, said ligand preferably comprises an alkylated nitrogen and/or quaternary ammonium ion or may be one of those described above.

25

30

35

20

The structural information on the crystals of the present invention can also be used for increasing or decreasing the affinity of a drug to a ligand-gated receptor. Such a method can comprise performing structure assisted drug design with the three-dimensional structure determined for the crystal, wherein said drug design is performed in conjunction with computer modeling; and modifying said drug to alter or eliminate a portion thereof suspected of interacting with a binding site of the binding cavity or with a non-specific binding site of the protein in the crystal. This method can, of course, be combined with one or more steps of any of the above described screening methods or other screening methods well known in the art. Methods for clinical compound discovery comprises for example ultrahigh-throughput screening (Sundberg, Curr. Opin. Biotechnol. 11 (2000), 47–53) for lead identification, and structure-based drug design (Verlinde and Hol, Structure 2 (1994), 577–587) and

-34

combinatorial chemistry (Salemme et al., Structure 15 (1997), 319–324) for lead optimization. Further information that could be taken into account for drug selection and design so far available for the localization of agonist and competitive antagonist binding sites on nicotinic acetylcholine receptors have recently been reviewed (Arias, Neurochem. Int. 36 (2000), 595-6450; Corringer et al., 1999). Once a drug has been selected, the method can have the additional step of repeating the method used to perform rational drug design using the modified drug and to assess whether said modified drug displays better affinity according to for example interaction/energy analysis.

10

15

20

25

35

A related method of the present invention for drug design comprises the step of using the structural coordinates of the water-soluble ligand-binding protein crystal comprising the coordinates of Table 1, to computationally evaluate a chemical entity for associating with the ligand-binding site or a non-specific binding site of a ligandbinding protein. This approach, made possible and enabled by this invention, is to screen computationally small molecule data bases for chemical entities or compounds that can bind in whole, or in part, to the AChBP. In this screening, the quality of fit of such entities or compounds to the binding site may be judged either by shape complementarity or by estimated interaction energy. Meng, et al., J. Coma. Chem. 13 (1992), 505-524. In addition, in accordance with this invention, AChBP mutants or chimerics may be crystallized in co-complex with known ligand-gated ion channel inhibitors. The crystal structures of a series of such complexes may then be solved by molecular replacement (for review see for example Brunger er al. Prog. Biophys. Mol. Biol. 72 (1999), 135-155; and references cited therein) and compared with that of wild-type AChBP. Potential sites for modification within the various binding sites of the Ilgand-binding domain may thus be identified. This information provides an additional tool for determining the most efficient binding interactions, for example, increased hydrophobic Interactions, between AChPB and a chemical entity or compound.

The design of compounds that bind to or inhibit ligand-gated ion channels according to this invention generally involves consideration of two factors.

First, the compound must be capable of physically and structurally associating with the ligand-binding domain. Non-covalent molecular interactions important in the association of the ligand-binding domain with its ligand include hydrogen bonding, van der Waals and hydrophoble interactions.

Second, the compound must be able to assume a conformation that allows it to associate with the ligand-binding domain. Although certain portions of the compound

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-35 ·

will not directly participate in this association, those portions may still influence the overall conformation of the molecule. This, in turn, may have a significant impact on potency. Such conformational requirements include the overall three-dimensional structure and orientation of the chemical entity or compound in relation to all or a portion of the binding site or the spacing between functional groups of a compound comprising several chemical entities that directly interact with the AChBP. If the theoretical structure of the given compound suggests insufficient interaction and association between it and AChBP, synthesis and testing of the compound is obviated. However, if computer modelling indicates a strong interaction, the molecule may then be synthesized and tested for its ability to bind to AChPB or a ligand-gated ion channel and functionally tested according to the methods mentioned above. In this manner, synthesis of inoperative compounds may be avoided. Once suitable chemical entities or fragments have been selected, they can be assembled into a single compound or inhibitor. Assembly may be proceed by visual inspection of the relationship of the fragments to each other on the three-dimensional image displayed on a computer screen in relation to the structure coordinates of AChBP. This would be followed by manual model building using software such as Quanta or Sybyl. Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include CAVEAT (Bartlett, et al. "CAVEAT: A Program to Facilitate the Structure-Derived Design of Biologically Active Molecules". In Molecular Recognition in Chemical and Biological Problems", Special Pub., Royal Chem. Soc. 78 (1989), 182-196); 3D Database systems such as MACCS-3D (Martin, J. Med. Chem. 35 (1992), 2145-2154) and HOOK (Molecular Simulations, Burlington, Mass.). Instead of proceeding to build an AChBP ligand in a step-wise fashion one fragment

or chemical entity at a time as described above, AChBP binding compounds may be designed as a whole or "de novo" using either an empty active site or optionally including some portion(s) of a known ligand(s). These methods include LUDI (Bohm, J. ComR. Aid. Molec. Design 6 (1992), 61-78); LEGEND (Nishibata and Itai, Tetrahedron 47 (1991), 8985); and LeapFrog (Tripos Associates, St. Louis, Mo.). Other molecular modelling techniques may also be employed in accordance with this invention; see, e.g., Cohen, J. Med. Chem. 33 (1990), 883-894 and Navia and Murcko, Current Opinions in Structural Biology 2 (1992), 202-210. Such computer modeling is preferably performed with a Docking program (Dunbrack

Methods for the identification of drugs or corresponding lead compounds in computational prescreen using X-ray crystal structures are described in the prior art

et al., Protein Sci. 6 (1997), 1661-1681 and Folding Des. 2 (1997), R27-R42).

-36

(Verlinde and Hol, Structure 2 (1994), 577–587; Kuntz, Science 257 (1992), 1078–1082; Shuker et al., Science 274 (1996), 1531–1534; Fejzo et al., Chem. Biol. 6 (1999), 755–769; WO 98/58961). The structural information can be consulted to efficiently optimize leads. Computational programs have been written to identify compounds ranging from very small molecules or functional groups (GRID: Goodford, J. Med. Chem. 28 (1985), 849–857; MCSS: Cafilsh et al., J. Med. Chem. 36 (1993), 2142–2167) to potential lead scaffolds (DOCK: Kuntz et al., Accounts Chem. Res. 27 (1994), 117–123) using solved X-ray crystal structures. Another method computationally prescreens compound libraries and experimentally tests the individual "hits" by X-ray crystallography (Verlinde et al., J. Comput. Aided Mol. Des. 6 (1992), 131–147) in order to decrease the size of the screening library. In addition, an experimental approach has been developed to find organic solvents that bind to active sites that may be recombined into a lead macromolecule (Allen et al., J. Phys. Chem. 100 (1996), 2605–2611).

15

20

25

10

5

Once a compound has been designed or selected by the above methods, the efficiency with which that compound may bind to the AChBP or a corresponding ligand-binding domain may be tested and optimized by computational evaluation. For example, a compound that has been designed or selected to function as an inhibitor must preferably demonstrate a relatively small difference in energy between its bound and free states (i.e., a small deformation energy of binding). Thus, the most efficient inhibitors should preferably be designed with a deformation energy of binding of not greater than about 10 kcal/mole, preferably, not greater than 7 kcal/mole. Inhibitors may interact with the ligand-binding domain in more than one conformation that is similar in overall binding energy. In those cases, the deformation energy of binding is taken to be the difference between the energy of the free compound and the average energy of the conformations observed when the inhibitor binds to the AChBP.

A compound designed or selected as binding to AChBP may be further computationally optimized so that in its bound state it would preferably lack repulsive electrostatic interaction with the target ligand-binding domain. Such non-complementary (e.g., electrostatic) interactions include repulsive charge-charge, dipole-dipole and charge-dipole interactions. Specifically, the sum of all electrostatic interactions between the ligand and the AChBP when the ligand is bound to AChBP, preferably make a neutral or favorable contribution to the enthalpy of binding. Specific computer software is available in the art to evaluate compound deformation

-37

energy and electrostatic interaction. Examples of programs designed for such uses include Gaussian 92, revision C (Frisch, Gaussian, Inc., Pittsburgh, Pa.); AMBER, version 4.0 (Kollman, University of California at San Francisco); QUANTA/CHARMM (Molecular Simulations, Inc., Burlington, Mass.); and Insight II/Discover (Biosysm Technologies Inc., San Diego, Calif.). These programs may be implemented, for instance, using a Silicon Graphics workstation, IRIS 4D/35, IBM RISC/6000 workstation model 550 or better a Unix workstation (SGI, Alpha, Sun, etc.) or any Linux PC. Other hardware systems and software packages will be known to those skilled in the art.

Once an AChBP-binding compound has been optimally selected or designed, as described above, substitutions may then be made in some of its atoms or side groups in order to improve or modify its binding properties. Generally, initial substitutions are conservative, i.e., the replacement group will have approximately the same size, shape, hydrophobicity and charge as the original group. It should, of course, be understood that components known in the art to alter conformation should be avoided. Such substituted chemical compounds may then be analyzed for efficiency of fit to AChBP by the same computer methods described in detail, above. As mentioned before, the above described methods of the present invention can also be used as an initial drug screening assay followed by a classical drug screening assay using the biochemical assays known in the art.

Methods for the preparation of compounds, chemical derivatives and analogues are well known to those skilled in the art and are described in, for example, Beilstein, Handbook of Organic Chemistry, Springer edition New York Inc., 175 Fifth Avenue, New York, N.Y.

25

30

35

10

15

20

In one embodiment of the method of the present invention the identified drug prevents or promotes correct assembly of a ligand-gated ion channel. Thus, the selected drug may for example either interfere with the contact regions of the monomers of the ligand-gated ion channel or may act as a scaffold for the assembly. In the latter case, the drug may be based for example on an antibody which binds to the contact regions of two or more monomers when assembled and thus facilitates the assembly process. Preferred contact regions with respect to the AChBP and the related nicotinic acetylcholine receptor are given below. In a still further embodiment of the above described methods, the drug can be selected such as to bind to a non-specific binding site of a ligand-gated ion channel. The non-specific binding site can for example include those contact regions that are highly conserved between the monomers of the ligand-gated ion channels.

. 10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-38

Once a drug has been selected in accordance with any one of the above described methods of the present invention, the drug or a pro-drug thereof can be synthesized in a therapeutically effective amount. As used herein, the term "therapeutically effective amount" means the total amount of the drug or pro-drug that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of a condition related to an ligand-gated ion channel, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. In addition or alternatively, in particular with respect to pre-clinical testing of the drug the term "therapeutically effective amount" includes the total amount of the drug or pro-drug that is sufficient to elicit a physiological response upon its binding to its target ligand-gated ion channel in an non-human animal test.

The present invention also relates to a drug produced by any one of the above described methods of the present invention, or a pro-drug thereof. Preferably, the drug or pro-drug thereof is present either alone or in a composition in a therapeutically effective amount.

The drug obtained by a method of the present invention may be characterized by its interaction with the binding sites in the binding cavity defined by the coordinates of crystal structure of the protein-ligand complex; for examples of such characterization see, e.g., US-A-5,798,247. Preferably, the drug, for example a potential inhibitor will form non-covalent bonds with one or more amino acids in the active site based upon the crystal structure. On the other hand, the drug may bind to a contact region of the individual monomers of the pentameric ligand-gated receptor. For example, multimer contact regions in *Lymnaea stagnalis* AChBP (SEQ ID No. 2) have been identified. Consecutive regions have at least every second residue involved in contacts with the other monomer. Contacts have been defined as 2 atoms within 4.2 angstrom distance in 2.7 Angstrom structure. The primary contact regions in mature AChBP (residues from A contacting B) are 15-21, 44-47, 85-87, 91-94, 122-124,143-146, 149, 185-187 and the complementary contact regions (from B contacting A, (identical to residues on A contacting E) are 3-4, 7-8, 11, 37-39, 53, 75-77, 96-104, 114-118, 163-170; see also Figure 14.

Thus, in one preferred embodiment the drug of the present invention interacts with a ligand-gated receptor comprising a pentamer with monomers A to E, wherein the drug binds to one or more primary contact regions of a monomer (residues from A contacting B) defined by amino acid residues 15 to 21, 44 to 47, 85 to 87, 91 to 94, 122 to 124, 143 to 146, 149, 185 to 187 of SEQ ID No. 2 and/or to one or more of the

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-39

complementary contact regions of the other monomer (from B contacting A, (identical to residues on A contacting E) defined by amino acid residues 3 to 4, 7 to 8, 11, 37 to 39, 53, 75 to 77, 96 to 104, 114 to 118 and 163-170 of SEQ ID No. 2; or to one of the contact regions identified in Figure 14; or to the corresponding contact regions of the monomers of a ligand-gated ion channel. Preferably, the ligand-gated ion channel is the nicotinic acetylcholine receptor and the order of the monomers is $\alpha\gamma\alpha\delta\beta$.

Any available method may be used to construct such model from the crystallographic and/or amino acid sequence data disclosed herein or obtained from independent analysis of crystalline AChBP proteins or other water-soluble ligand-binding proteins of the present invention. Such a model can be constructed from available analytical data points using known software packages such as HKL, MOSFILM, XDS, CCP4, SHARP, PHASES, HEAVY, XPLOR, TNT, NMRCOMPASS, NMRPIPE, DIANA, NMRDRAW, FELIX, VNMR, MADIGRAS, QUANTA, BUSTER, SOLVE, O, FRODO, RASMOL, CNS, REFMAC, ARP/WARP, XTALVIEW and CHAIN. The model constructed from these data can then be visualized using available systems, including, for example, Silicon Graphics, Evans and Sutherland, SUN, Hewlett Packard, Apple Macintosh, DEC, IBM, and Compaq. The present invention also provides for devices such as a computer system which comprises the model of the invention and hardware used for construction, processing and/or visualization of the model of the invention. Further embodiments provide a computer system comprising computer hardware and the model of the present invention. The study of the interaction of the candidate species with the model can be performed using available software platforms, including QUANTA, RASMOL, O, CHAIN, FRODO, INSIGHT, DOCK, MCSS/HOOK, CHARMM, LEAPFROG, CAVEAT (UC Berkley), CAVEAT (MSI), MODELLER, CATALYST, XTALVIEW and ISIS. Computer readable media such as floppy discs, CD ROMs, tapes, and any other storage or processing means comprising crystallographic and/or nucleotide/amino acid sequence data disclosed herein or obtained from independent analysis of crystalline AChBP proteins or other water-soluble ligand-binding proteins of the present invention are subject of the present invention as well. Any one of the mentioned means and devices can advantageously be used for modeling an antagonist/inhibitor or agonist/activator of a ligand-gated receptor.

Furthermore, the present invention relates to the construction of theoretical three dimensional (3D) models of ligand-binding domains of ligand-gated ion channels by computer-assisted molecular modeling using the X-ray coordinates of the water-soluble ligand-binding proteins of the invention. These 3D models can correspond

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-40

either to the entire ligand-binding domain (~220 to 240 extracellular amino acids) or may be limited to the ligand-binding site.

The concept of using 3D structures of the mollusc ligand-binding proteins for molecular modeling and tool for structure prediction of for example mammalian, in particular human ligand-gated ion channels gains support from the observation that the ligand-binding domain of vertebrate glutamate receptor channels and bacterial periplasmic substrate-binding proteins (PBPs) share similar 3D structures despite the very low sequence similarity between ionotropic glutamate receptor subunits and the PBPs that were used as templates (12%); for review see Paas et al. TiPS 21 (2000),

10 87-92 and refernces cited therein

Thus, on the basis of a computer-assisted molecular modeling, optionally supplemented by for example functional studies of site-specific mutants, the crystal structure of the ligand-binding domain of ligand-gated ion channels and theoretical 3D models of these domains can be predicted. In turn, these models can be used for structure assisted drug design. The predicted models may be further refined, for example by monitoring the effects of mutations of amino acid residues that are probably located in the ligand-binding site on (1) agonist-elicited channel activation and desensitization, (2) inhibition of channel activity by various competitive receptor antagonists; or (3) the binding of various ligands. Experimental setups for analyzing such effects are known to the person skilled in the art, see also the documents cited for functional assay systems of ligand-gated ion channels.

Thus, the embodiments of the present invention enable various possibilities for identification and modeling new ligands of ligand-gated ion channels as well as modifying the ion channels themselves. Accordingly, the present invention relates to the use of the above described polynucleotides, proteins, dimers and pentamers, ligand-gated ion channels, vectors, host cells, antigens, antibodies, oligonucleotide probes, crystals, their structural coordinates and methods for screening or profiling putative ligands of ligand-gated receptors.

Methods for the lead generation in drug discovery using proteins and detection methods such as mass spectrometry (Cheng et al. J. Am. Chem. Soc. 117 (1995), 8859–8860) and some nuclear magnetic resonance (NMR) methods (Fejzo et al., Chem. Biol. 6 (1999), 755–769; Lin et al., J. Org. Chem. 62 (1997), 8930–8931).

The newly identified drug obtained by a method of the present invention, i.e. an antagonist/inhibitor or agonist/activator can be used for the preparation of a pharmaceutical composition for the treatment of a ligand-gated ion channel mediated or related disorder. Such disorders are well know to the person skilled in the art. For

WO 01/58951 PCT/EP01/01457

-41

example, possible applications of agonist and antagonists to nAChRs are based on their participation in complex functions such as attention, memory, and cognition, and their involvement in the pathogenesis of certain neuropsychiatric disorders (Alzheimer's and Parkinson's diseases, Tourette's syndrome, schizophrenia, depression, etc). For the majority of these disorders, the use of nAChRs' agonists may represent either a prophylactic (esp. for Alzheimer's and Parkinson's diseases) or a symptomatic treatment; for review see for example Mihailescu and Drucker-Colin, Arch. Med. Res. 31 (2000), 131-144.

The medicinal chemistry and molecular biology of GABA-activated ligand-gated ion channels also in terms of agonist and antagonist structural profiles is described in Chebib et al., J. Med. Chem. 43 (2000), 1427-1447.

Glycine receptors and disorders of glycinergic neurotransmission are extensively reviewed in Rajendra et al., Pharmacol. Ther. 73 (1997), 121-146 and Barry et al., Clin. Exp. Pharmacol. Physiol. 26 (1999), 935-936.

The central role of 5-HT3 receptor in CNS disorders and 5-HT3 receptor antagonists are described in Bloom and Morales, Neurochemical Research 23 (1998), 653-659 and Higgins and Kilpatrick, Expert Opin. Invest. Drugs 8 (1999), 2183-2188.

In one embodiment, the antagonist/inhibitor is or is derived from a protein, an antigen, antibody or from a toxin of the ligand-gated ion channel. Likewise, the agonist/activator can be derived from a protein, an antigen, antibody or from a toxin of the ligand-gated ion channel. Possible starting points comprise for example peptide toxins, e.g., conotoxin (IMI) and alpha bungarotoxin, lophotoxins (Bippinatins), tubocurarine, decamethonium, alpha-cobratoxin, epibatidine, acetylcholine, choline, nicotine, carbachol, serotonin or GABA. The structure of these molecules together with that of the crystal of the target ligand-binding domain can be used to model the compound and elucidate side chains, functional groups etc. which may be added, deleted or modified in order to improve for example affinity and/or specificty of the drug or for example make a drug which acts on a different target non-reactive with a certain ligand-gated ion channel.

In a preferred embodiment for the uses according to the present invention, the ligand-gated ion channel is the nicotinic acetylcholine receptor and said mediated or related disorder is Tourette's syndrome, Alzheimer's disease, addiction to nicotine or schizophrenia.

35

20

25

30

As mentioned herein before, this is the first time it could be shown that water-soluble ligand-binding proteins exists in molluscs, which closely resemble the ligand-binding

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-42

domain of ligand-gated ion channel of higher mammals. It is expected that similar ligand-binding proteins exist in other molluscan species or even in the lineage the Mollusca, Protostomia, Coelomata, Bilateria, Eumetazoa, Metazoa, Fungi/Metazoa group. Accordingly, the present invention also relates to the use of a ligand of a ligand-gated ion channel for identifying and isolating a water-soluble ligand-binding protein from such species, preferably from a mollusc. Preferably, the ligand used for the isolation of the protein is α -bungarotoxin. The water-soluble ligand binding proteins obtainable from these organisms as well as derivatives that can be made in accordance with the teaching present herein are also subject of the present invention.

Furthermore, for the first time the crystal structure of a nicotinic binding site has been revealed. This crystal structure shows that the molluscan AChBP is a homolog of the LGIC superfamily ligand binding domains. It reveals the Ig-topology, the location of the binding site at the subunit interface, the position of the MIR and the extensive data on the nicotinic ligand binding residues. Importantly, it gives important new information about the exact fold and the arrangement of the nicotinic ligand-binding site in three dimensions. It shows the presence of a second pocket that has been noticed by EM analysis. Furthermore, it clarifies the arrangement of subunits by showing the relative positioning of the principal and complementary part of the ligand-binding site. It provides an explanation of the role of the LGIC superfamily conserved residues in stabilizing the monomer structure by the formation of hydrophobic cores and packing of secondary structure elements and it makes clear how the pentamers are built up, and how weakly the pentamer interfaces are conserved between LGICs.

This structure can be used for the numerous drug-design studies that are targeting the LGIC superfamily. The general structural knowledge on its folding will be applicable to the GABA, serotonin (5HT₃) and glycine receptor fields. It will help to understand their ligand-binding characteristics and could thus have impact on development of e.g. anti-emetics aimed at the 5HT₃ receptor or the mood-defining drugs that target the GABA receptors. However, the availability of a three-dimensional description of the nicotinic ligand-binding site will be especially relevant for the design of new drugs against Alzheimers' disease, epilepsy and the addiction to smoking which have the neuronal nicotinic receptors as their targets.

Many embodiments and the examples feature the acetylcholine-binding protein (AChBP) of the invention and the embodiments generally described herein are

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-43

preferably related to the nicotinic acetylcholine receptor (nAChR), more preferably to the alpha subunit, and most preferably to the alpha 7 subunit. However, it should be understood that all embodiments equally apply to the other water-soluble ligand-binding proteins and generally to the ligand-gated ion channels mentioned herein. For example, the crystal structure of the AChBP can be used to model new ligands for the acetylcholine receptor, preferably such with inhibiting or stimulating action on the acetylcholine receptor. Likewise, it is possible to identify and model new ligands for other ligand-gated ion channels (including glycine, GABA and serotonin receptor) with inhibiting action. Such ligands may for example prevent correct assembly of ligand gated ion channels. Preferably such ligands prevent correct assembly of specific sub types of ligand gated ion channels. On the other hand, ligands can be identified and modeled that promote correct assembly of ligand gated ion channels, preferably of specific sub types of ligand gated ion channels. As mentioned before, the methods of the present invention also allow modeling inhibitors for the non-specific binding site of ligand gated ion channels.

In addition, it is possible to predict and create mutants and chimeras of AChBP with modified assembly behaviour, modified ligand binding behavior such as with increased resemblance of the binding site to the acetylcholine receptor subtype on the primary binding site and generally with increased resemblance to particular ligand-gated ion channels in activity and conformational changes. In view of the closest relationship between AChBP and the acetylcholine receptor it is particular preferred to create mutants and chimeras with increased resemblance of the binding site to the acetylcholine receptor subtype on the secondary binding site. However, the prediction and creation of mutants and chimeras with increased resemblance of the binding site to other ligand gated ion channels subtype on the primary binding site or on the secondary binding site are envisaged as well.

These and other embodiments are disclosed and encompassed by the description and Examples of the present invention. Further literature concerning any one of the antibodies, methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries and databases, using for example electronic devices. For example the public database "Medline" may be example under which is available on the Internet, for http://www.ncbi.nlm.nih.gov/PubMed/medline.html. **Further** databases and http://www.ncbi.nlm.nih.gov/, http://www.infobiogen.fr/. addresses, such as http://www.fmi.ch/biology/research_tools.html, http://www.tigr.org/, are known to the person skilled in the art and can also be obtained using, e.g., http://www.lycos.com.

-44

An overview of patent information in biotechnology and a survey of relevant sources of patent information useful for retrospective searching and for current awareness is given in Berks, TIBTECH 12 (1994), 352-364.

- This disclosure may best be understood in conjunction with the accompanying drawings, incorporated herein by references. Furthermore, a better understanding of the present invention and of its many advantages will be had from the following examples, given by way of illustration and which are not intended as limiting.
- Unless stated otherwise in the examples, all recombinant DNA techniques are performed according to protocols as described in Sambrook et al. (1989), Molecular Cloning: A Laboratory Manual. Cold Spring Harbor Laboratory Press, NY or in Volumes 1 and 2 of Ausubel et al. (1994), Current Protocols in Molecular Biology, Current Protocols. Standard materials and methods for plant molecular work are described in Plant Molecular Biology Labfase (1993) by R.D.D. Croy, jointly published by BIOS Scientific Publications Ltd (UK) and Blackwell Scientific Publications (UK).

20 Brief description of the drawings

Figure 1: Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences. The AChBP alignment was made using "ClustalX_1.8" (Thompson et al., Nucleic Acids Research 24 (1997), 4876-4882. The subsequent alignment was further processed using "Genedoc" version 2.5.000 (Nicholas et al. (1997) Genedoc a tool for editing and annotating multiple sequence alignments). Identical amino acids are indicated with "*", equivalent amino acid with ":", and similar amino acids with ".". Glycosylation sites are Asn 66 for L-AChBP and Asn 21 and 26 for B-AChBP in the amino acid sequence of the respective mature AChBP SEQ ID No. 2 and 4, and 6 and 8, respectively.

Figure 2: Hydrophobicity plots of the mature AChBP amino acid sequences. The B&L-AChBP hydrophobicity plots were made using "Protein sequence analyses" according to the method described in Kyte and Doolite (J. Mol. Biol. 157 (1982), 105-132). 2A: L-AChBP_T1 (SEQ ID No. 2), 2B: L-AChBP_T2 (SEQ ID No. 4), 2C: B-AChBP_T1 (SEQ ID No. 6), 2D: B-AChBP_T2 (SEQ ID No. 8).

PCT/EP01/01457

WO 01/58951

-45

Figure 3:

5

10

Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences with the amino acid sequences of the ligand-binding domains of the ligand-gated receptors nAChR-α7, GABAAR-β1, 5-HT3R and GlyR-α1. Sequence alignment and processing was performed as described for Figure 1. The accession numbers of the amino acid sequences used for the alignment are as follows: Human alpha1: Human alpha7: Y08420; Human 5HT3: CAA06442; Human GlyR_alpha1: S12382; Human GABA_b1: NP_000797. A similar sequence alignment can be performed with the corresponding rat (ratnAChRa7_Q05941, rat5HT3R_P35563, sequences ratGABARb1_P15431, ratGlyRa1_p24524) which will substantially similar if not identical results.

15 Figure 4:

Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences with the amino acid sequences of nAChRs. Sequence alignment and processing was performed as described for Figure 1. The accession numbers of the amino acid sequences used for the alignment are as follows: Human alpha1: ACHUA1; Human alpha2: AAG23253; Human alpha3: A53956; Human alpha4: P43681; Human alpha5: P30532; Human alpha6: Q15825; Human alpha7: Y08420; Human alpha9: CAB65091. A similar sequence alignment can be performed with the corresponding rat sequences (ratnAChRa7_Q05941, rnAChRa9_P43144, rnAChR2_P1238, rnAChRa3_P04757, rnAChRa4_P09483) which will give substantially similar if not identical results.

25

20

Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences with the amino acid sequences of nAChRs alpha 1 and 7. Sequence alignment and processing was performed as described for Figure 1. The accession numbers of the amino acid sequences used for the alignment are as follows: Human alpha1: ACHUA1; Human

alpha7: Y08420. A similar sequence alignment can be performed with

Figure 5:

WO 01/58951

PCT/EP01/01457

-46

the corresponding rat sequence ratnAChRa7_Q05941 which will give substantially similar if not identical results.

5 Figure 6:

10

15

20

The pentameric structure of AChBP. a In this schematic representation each monomer has a different grey level. Subunits are labeled anticlockwise, with A-B, B-C, C-D, D-E and E-A forming the plus and minus interface side, with the principal and complementary ligand-binding sites respectively (ball-and-stick representation). b Viewing the AChBP pentamer perpendicular to the five-fold axis. The equatorially located ligand-binding site (ball-and-stick representation) is highlighted only in the A (light) and B (dark) interface.

Figure 7:

The AChBP monomer. Ribbon representation of the AChBP monomer. The secondary structure starting from the N-terminus (top) towards the C-terminus (bottom). The monomer is viewed towards the center of the pentamer. In the nAChR, the top would correspond to the N-terminus of the ligand binding domain, pointing towards the synaptic cleft, while the C-terminus would be entering the membrane at the bottom, continuing into the transmembrane domain. The AChBP monomer is built up mainly of β-strands, except for an N-terminal ⟨-helix. It contains 14 β-strands that are organized in the two antiparallel β-sheets, with an immunoglobulin topology. However, in contrast to the classical immunoglobulin fold, the AChBP β-sheets are rotated against each other, forming a small pocket, as visible in Figure 6.

25

Figure 8:

The ligand-binding site at dimer interface. Ribbon representation of two neighboring AChBP monomers. Monomer A is shown in grey and monomer B in dark grey. The ligand-binding site is located at the interface between two monomers. As predicted for the nAChRs, the acetylcholine binding site in AChBP occurs at the interface between two neighboring subunits. Similar to the model proposed for the nAChRs, the ligand-binding site is asymmetric, formed mainly by aromatic residues. Residues from mature AChBP monomer A (TyrA89, TrpA143, TyrA185, CysA187, CysA188 and TyrA192) form the principal component, while residue TrpB53 from monomer B

35

WO 01/58951

PCT/EP01/01457

-47

creates the complementary part of the ligand-binding site. There are five identical ligand-binding sites in the AChBP pentamer, similar to the homomeric $\alpha 7$ neuronal receptor.

5 Figure 9:

The ligand binding site. Stereo figure showing the ligand binding site in AChBP, at the interface of two monomers. Residues from mature AChBP monomer A (TyrA89, TrpA143, TyrA185, CysA187, CysA188 and TyrA192) form the principal component, while residue TrpB53 from monomer B creates the complementary part of the ligand-binding site with with additional residues ArgB104, LeuB112 and MetB114. There are five identical ligand-binding sites in the AChBP pentamer, similar to the homomeric α7 neuronal receptor.

Figure 10:

15

Multiple sequence alignment of AChBP amino acid sequences with indication of secondary structure and solvent accessibility derived from the crystal structure. Alignment of the four molluscan AChBP sequences, with secondary structure and solvent accessibility of the Lymnea stagnalis AChBP-1 indicated from the crystal structure. The Figure was prepared with ESPript (Gouet et al., Bioinformatics. 15 (1999), 305-308), using DSSP (Kabsch and Sander, Biopolymers. 22 (1983), 2577-2637). Under the alignment the solvent accessibility is indicated, white most buried, dark blue most exposed, according to ESPript defaults (blue A> 0.4, cyan 0.1<A<0.4, white A<0.1).

20

10

25 Figure 11:

Sequence alignment of AChBP with LGICs. The alignment shows only the N-terminal domain of the LGIC subunits and is based on a multi-sequence alignment of 92 full-length LGIC sequences. Abbreviations used, H and Tca, stand for human and *Torpedo californica*. Secondary structure elements (α : α -helix, β : β -strand, η : 3_{10} -helix) are indicated above the sequence, in accordance with Fig 12a. AChBP shares 23% sequence identity with the ligand-binding domain of human α_7 . The LGIC conserved residues (bold, grey background) are displayed. Beginning and end of the Cys-loop are indicated by a "**". Nicotinic receptor ligand-binding residues on the principal and complementary side are indicated.

30

PCT/EP01/01457

WO 01/58951

-48

Figure 12:

Overview of the AChBP monomer structure. **a** Stereo representation of the AChBP monomer as viewed from outside the pentameric ring. Disulfide bridges are indicated in ball-and-stick representation. In a complete ion-channel the N-terminus would be pointing towards the synaptic cleft, while the C-terminus would enter the membrane at the bottom, continuing into the first transmembrane domain. **b** Topology diagram of the AChBP monomer. For comparison with Ig-folds the strands have been labeled a-g, showing the additional strand (b') and hairpin (f'-f"). In this structure, strands have been labeled β 1- β 10 with loops (or turns) L1-L10 preceding each strand with the same number. The β 5 strand is broken (β 5- β 5') with internal loop L5', β 6 also has a small break, but is shown continuously; (see Fig. 11). The precise beginnings and ends of strands may change slightly with increasing resolution, but the topology seen here will be highly conserved across the entire family of LGICs.

15

20

10

5

Figure 13:

The ligand-binding site. **a** Stereo representation of the ligand-binding site in ball-and-stick representation, showing the contribution of the principal A (TyrA89/ α_1 Tyr93), B (TrpA143/ α_1 Trp149) and C (TyrA185/ α_1 Tyr190, CysA187/ α_1 Cys192, CysA188/ α_1 Cys193, TyrA192/ α_1 Tyr198) and the complementary D (TrpB53/ γ Trp55, GlnB55/ γ Glu57), E (ArgB104/ γ Leu109, ValB106/ γ Tyr111, LeuB112/ γ Tyr117, MetB114/ γ Leu119) and F (TyrB164) 'loops'. **b** Stereo view of the electron density map displaying a HEPES buffer molecule in the ligand-binding site. This experimental density (contoured at 1 σ) is derived from cross-crystal averaging. **c** Location of the principal ligand-binding residues on the monomer. **d** Location of the complementary ligand-binding residues on the monomer. (orientation as in Figure 6b)

25

30 Figure 14:

Dimer interface a Stereo figure of the dimer interface. Representation of the interface residues (ball-and-stick) on a schematic secondary structure figure. The figure shows the plus face of subunit A and the minus minus face of subunit B b Dimer interface interactions. Note that due to the low conservation of these interfaces (Fig. 11) the actual interactions will not be conserved in any LGIC interface, but that in all receptors the topological regions are likely to form the interface.

WO 01/58951

PCT/EP01/01457

-49

Figure 15:

Conservation in the LGIC superfamily. Conserved residues are indicated on the top, middle and bottom respectively on the monomer as viewed from the central pore. The hydrophilic conserved residues are indicated in dark. Conserved residues are indicated as viewed from the central pore. Hydrophobic Cluster I: residues 6, 10, 63, 65, 71, 81, 105, 111; Cluster II: residues 20, 27, 29, 31, 58, 82, 84, 86, 140, 150, 152, 195; Cluster III: residues 33, 35, 38, 41, 48, 52, 125, 138, 171, 173, 199, 201. The hydrophilic conserved residues: Asp60, Asp85, Asn90, Gly109, Cys123, Cys136, Lys203. Conserved residues in the ligand binding site: 106, 145, 192. These three and Lys203 are the only conserved residues without structural role in the monomer. Note how very few conserved residues are at the surface. Within the LGIC family the Cys-loop residues are also highly conserved; see bottom, left.

10

WO 01/58951

5

10

15

20

30

35

PCT/EP01/01457

-50 **EXAMPLES**

EXAMPLE 1: Isolation of Lymnaea AChBP from the CNS, determination of mass and N-terminal protein sequence

Isolation: 80 CNS of Lymnaea were homogenized in lysis buffer (PBS [16 mM Na₂HPO₄, 4 mM NaH₂PO₄, pH 7.4; 150 mM NaCl] 0.5% Nonidet P-40; 0.1% triton, 0.2% tween-20) containing 1 ug/ml aprotinin, 10 ug/ml benzamidine, 0.5 ug/ml leupeptin, 24 ug/ml pefabloc. The CNS lysate was cleared by triplicate centrifugation at 12,000x g for 5 min. Streptavidin-coated magnetic beads (Dynal, Oslo), 5 mg, were saturated with α-bungarotoxin conjugated to Biotin (4 ug) (Molecular Probes, Oxford, UK). These beads were washed in PBS to remove excess α-bungarotoxin, then added to the cleared CNS lysate, and incubated for 1 h. After this, beads were washed 3 times in PBS to remove unbound protein. A control reaction without α-bungarotoxin was performed. Proteins bound to α-bungarotoxin were allowed to elute off in 10 μl of PBS containing 10-4 M nicotine for 1h.

Mass determination: The eluent was separated on a microcolumn LC system was similar to that described previously (Hsieh et al.; Anal. Chem. 70; 1998; 1847-1852). A commercial syringe pump (Perkin-Elmer /ABI, model 140B) was used to deliver a flow rate of 20 μl /min to the column. After loading of sample to the column the flow rate was dropped to 10 μl /min. The eluent was then switched from 0.2% acetic acid to 0.2% acetic acid/ 60% acetonitril in 1 min. Electrospray mass spectra in MS mode were acquired on a Micromass Q-TOF quadropole time-of-flight mass spectrometer equipped with a Z-spray atmospheric pressure ionization source.

Protein sequence analysis: For sequence analysis α-bungarotoxin binding protein was extracted using the same procedure, now followed by SDS-PAGE and Western Blotting on PDVF membrane. Sequence analysis was performed with Edman degradation of the 24 kDa blotted protein (apparent MW) using a protein sequencer (ABI, Perkin Elmer).

EXAMPLE 2: Cloning the Lymnaea AChBP cDNA sequence: PCR and screening of a cDNA library

PCR cloning: A degenerate oligonucleotide was synthesized based on the amino acid sequence LDRADILYNI (SEQ ID No. 10), residues 1-10, of AChBP, (5'-CGGATCCGA(TC)(AC)GIGC(GATC)GA(TC)AT(ATC)(TC)T(GATC)TA(TC)AA(TC)A T-3'; SEQ ID No. 11), containing a BamHI restriction site, and used in combination with a primer on the IZAPII lambda vector. PCR was performed on a IZAP II cDNA

-51

library of the Lymnaea CNS, in a 100 μl reaction volume with 1.0 unit of Super Taq DNA polymerase (Boehringer Mannheim, Germany) in a DNA thermal cycler (Perkin-Elmer Cetus, CT) using 45 cycles of (94 °C, 20 sec; 53 °C, 30 sec; and 72 °C, 1 min. Amplified cDNA was digested with BamHI and EcoRI, separated on agarose gel, and a product of ~900 bp was cloned and sequenced. Library screening: Approximately 20,000 clones of the amplified lambda ZAP II CNS cDNA library were plated at a density of 10⁵ pfu/400 cm² and absorbed to charged Nylon membranes (Boehringer Mannheim, Germany). The AChBP PCR product was used as a random primed probe, labeled with [alfa32P]dATP (specific activity >109 cpm/mg). Membranes were hybridized in 6x SSC (1x SSC; 0.15 M NaCl and 0.015 M Na-citrate), 0.2% SDS, 5x Denhardts and 10 ug/ml herring sperm DNA at 65 °C for 18 h. The filters were washed in 0.2x SSC, 0.2% SDS, at 65 °C for 30 min, and autoradiographed. Four individual cDNA clones were in vivo excised, and sequenced using dideoxy chain termination in both orientations. Two types of sequence were obtained, named L-AChBP_T1 and L-AChBP_T2. The signal sequences were determined with "SMART", Simple Modular Architectur Research Tool (V3.1); see Schultz et al., Proc. natl. Acad. Sci. USA 95 (1998), 5857-5864 and Nucleic Acids

20

25

30

35

could experimentally be confirmed.

5

10

15

EXAMPLE 3: Lymnaea AChBP-related sequences: cloning of the Bulinus truncatus cDNAs

Res. 28 (2000), 231-234. In case of L-AChBP_T1 (SEQ ID No. 2) the prediction

Total RNA was isolated from Bulinus brain ganglia (CNS), and reverse transcribed into hexanucleotide primed cDNA. Two degenerate oligonucleotides, directed to the forward primer: 5'-Lymnaea AChBP_T1 sequence, GCGAATTCGAYACIGARWSIGGNGCNACNTG-3' (SEQ ID No. 12), reverse primer: 5'-GCGAAGCTTCRTCYTCRTAIGCYTCNGCRCARC-3' (SEQ ID No. 13), were used to amplify AChBP-related sequences. PCR was performed on one animal equivalent of CNS cDNA using 150 pmole of each primer under standard conditions for 45 cycles (94'C, 20 sec; 54' C, 30 sec; 72 'C, 1 min). Amplified cDNA was EcoRI/HindIII digested, cloned into EcoRI/HindIII digested pBluescript, and sequenced. The ORFs of the obtained sequences showed a Bulinus AChBP, sequence-related to Lymnaea AChBP, named B-AChBP_T1. This partial cDNA was used to screen a Bulinus brain cDNA library using the same hybridization protocol as described for the cloning of the Lymnaea cDNAs, and yielded two cDNA clones, encoding B-AChBP_T1 and B-AChBP_T2. Sequencing of the cDNAs was performed in both orientations.

WO 01/58951

10

15

20

25

30

35

PCT/EP01/01457

-52

EXAMPLE 4: The production of L-AChBP-T1 and -T2 and B-AChBP-T1 and -T2 in the yeast Pichia pastoris and functional characterization

5 Production of recombinant AChBP:

In order to produce L-AChBP_T1 and T2 and B-AChBP_T1 and T2 as recombinant proteins in the Pichia pastoris expression system (Pichia Expression Kit version 3.0, Invitrogen), the DNA sequence encoding the mature form of these proteins (see sequence files) was cloned into the pPIC9 expression vector (Invitrogen). The mature sequences of L-AChBP_T1, T2 and B-AChBP_T1 and T2 were PCR amplified (using Pfu-taq DNA polymerase (Stratagene) in order to avoid introduction of errors into the sequence due to PCR) and restriction sites were added to the primers to allow rapid pPIC9 compatible cloning. The amplified sequence of mature AChBP_T1 and T2 were Xhol/EcoRl inserted into pPIC9, whereas L-AChBP_T2 and B-AChBP_T1 and T2 were Xhol/EcoRl inserted into pPIC9 (the alpha-mating factor cleavage site was fully reconstructed after Xhol digestion).

Constructs with and without an additional C-terminal His-tag (SRGHHHHHH (SEQ ID No. 14) in the case of L-AChBP_T1, EFKDDDDKHHHHHHH (SEQ ID No. 15) otherwise) were generated for each of the AChBP (sub)types. The AChBP/pPIC9 constructs were amplified in E. coli DH5 α F and isolated and purified using the plasmid Maxi Kit (Qiagen). Due to the engineered cleavage site at the N-terminus of the amino acid sequence four additional amino acids (EAEA, SEQ ID No. 16) will precede the N-terminus of the original mature protein. Prior to transfection into Pichia pastoris the constructs were linearised (for protocol see supplier's manual; Pichia Expression Kit version 3.0, Invitrogen) and subsequently purified phenol/chloroform extraction, and ethanol precipitation. Approximately 5 µg of each of the linearised constructs was transformed into freshly prepared electro-competent Pichia pastoris cells and plated onto MD plates (for protocol see supplier's manual; Pichia Expression Kit version 3.0, Invitrogen corporation). Electrocompetent Pichia pastoris cells were aquired according to the protocol provided by Invitrogen. Plates were incubated at 30°C until the appearance of Pichia colonies, which were subsequently analysed for the presence of the correct insert by PCR amplification (for protocol see supplier's manual; Pichia Expression Kit version 3.0, Invitrogen). Colonies containing an homologous recombination with the Pichia genome, carrying the AChBP sequence, were grown in 25 ml of BMGY for 1-2 days (30°C; rotation at 250rpm), after which the cells were centrifuged (10 min., 1500g) and the cell pellet was resuspended into 10 ml of BMMY. Growth (30°C, 250rpm) was continued for an

15

20

25

WO 01/58951 PCT/EP01/01457

-53

additional 4 days (day 3-6), during which the expression of AChBP was induced by the addition of 100% methanol (1% of total culture volume) once every 24 hours. At day seven the culture was centrifuged (15 min.; 2000g; 4°C) and the medium was collected. The AChBP expression level of the various cultures was determined by the analyses of a fraction of the collected medium with SDS-polyacrylamide gel electrophoresis (see suppliers manual; Pichia Expression Kit version 3.0, Invitrogen). The cultures that yielded the highest level of AChBP expression were selected and stored as glycerol stocks.

Recombinant AChBP that contained a C-terminal His-tag was isolated and purified from the Picha pastoris medium using Talon metal affinity resin (according to protocol as described within the user manual; Clontech laboratories Inc.). The protein concentration was subsequently analysed using SDS-polyacrylamide gel electrophoresis and reference marker proteins. Polyclonal antibodies have been raised successfully to the recombinant L-AChBP_T1 and B-AChBP_T1 proteins in Balb-C mice. Immune-sera were obtained without crosslinking of the proteins.

Binding characteristics of AChBP:

First the binding curve of α -Bungarotoxin to His-tagged AChBP was determined, and an affinity of 3.5 nM was calculated. Using α -Bungarotoxin in a competitive binding assay ligands of several types of ligand-gated ion channels were then tested on Histagged AChBP, i.e., ACh, serotonin, GABA, glycine, and glutamate. Both ACh and serotonin did compete with α -Bungarotoxin binding at 4.2 mM and 269 mM, IC50s respectively. GABA, Glycine and glutamate did not compete for binding with α -Bungarotoxin. Thus, as predicted by the primary sequence and by subunit structure also the ligand-binding characteristics of AChBP resembled that of a nAChR.

In a second series of competitive binding assays the ligand binding characteristics of AChBP were studied in more detail, now using various agonists and antagonists of the AChRs. Nicotine a classical agonist of the nAChRs, is a high affinity ligand of Histagged AChBP (IC50 98 nM). Epibatidine, a high affinity agonist of the nAChRs, also binds with high affinity to His-tagged AChBP (IC50 1.4 nM), which is even higher than the 58 pM affinity of epibatidine reported for the nAChR (Badio, Mol. Pharmacol. 45 (1994), 563-569). Other cholinergic agonists bind with a lower affinity e.g., decamethonium, carbachol, and choline respectively with IC50s of 4.1 μ M, 43 μ M. and 190 μ M. Summary of affinities indicated in Table 2.

WO 01/58951

15

20

25

PCT/EP01/01457

-54

Table 2

	IC50 (μM)	nHill		IC50 (μM)	nHill
serotonin	269 ± 67	0.65 ± 0.03	α-cobratoxin	16.2 ± 0.1	4.08 ± 0.30
choline	190 ± 32	0.91 ± 0.20	atropine	5.25 ± 0.49	1.91 ± 0.23
carbachol	43 ± 2.7	0.67 ± 0.05	decamethonium	4.1 ± 0.3	1.13 ± 0.09
acetylcholine	4.2 ± 1.1	0.72 ± 0.09	physostigmine	1.25 ± 0.04	0.66 ± 0.07
nicotine	0.098 ± 0.025	0.78 ± 0.05	d-tubocurarine	0.093 ± 0.003	0.83 ± 0.04
epibatidine	0.0014 ± 0.0001	0.66 ± 0.04	gallamine	0.039 ± 0.007	0.71 ± 0.14
			α-bungarotoxin	0.0026 ± 0.0006	0.80 ± 0.18

5 Competition-binding of typical antagonists of the nAChRs, e.g., tubocurarine and α-Bungarotoxin, have a high affinity for His-tagged AChBP, respectively IC50s of 93 nM and 2.6 nM. The cholinergic antagonist succinylcholine has a very low affinity for His-tagged AChBP (IC50 7.9 mM). Interestingly, also muscarinic receptor antagonists bind to His-tagged AChBP with relatively high affinity, e.g., the muscarinic allosteric modulator gallamine (IC50 39 nM), and the muscarinic antagonist atropine (IC50 5.3 mM). Physotigmine which is a known blocker of acetylcholinesterase and is also an antagonist of the nAChR, binds to His-tagged AChBP with an IC50 of 1.3 mM.

Finally, Bipinnatin-B was tested, a synthetic form of the coral lophotoxin on AChBP (Groebe and Abramson, J. Biol. Chem. 270 (1995), 281-286). Bipinnatin-B is a general blocker of nAChRs and is known to covalently bind to Tyr-190 of the α subunits (Abramson, J. Biol. Chem. 263 (1988), 18568-18573). His-tagged AChBP was incubated with the toxin, and the mass of the protein increased with 430.1 Da, corresponding well to the calculated mass of Bipinnatin-B of 431 Da, indicating that the toxin also binds to Tyr-184 in His-tagged AChBP.

EXAMPLE 5: Expression and purification of recombinant AChBP for crystallization

The AChBP_T1 protein from Lymnea stagnalis (AChBP) was overexpressed in Pichia pastoris GS115 strain using the AOX1 gene expression system from Invitrogen. Media and methods used for AChBP expression are also described in Invitrogen manual Pichia Expression Kit. For long term storage the transformants were grown overnight in YPD medium at 30°C.

-55

YPD or Yeast Extract Peptone Dextrose medium

1% yeast extract (Difco)

2% peptone (Difco)

2% dextrose (glucose) (Merck)

5 The cells were harvested and suspended in YPD medium containing 15% glycerol at final OD600 of ~50. The cells were frozen in a dry ice/ethanol bath and stored in the freezer (Revco) at –80°C. Normally, the expression of AChBP started with plating the cells from the glycerol stock on MD plate.

MD or Minimal Dextrose Medium

10 1.34% YNB (yeast nitrogen base w/o amino-acids) (Difco)

4x10-5 % d-biotin (Sigma)

1% dextrose

For plates add 15g of agar (Difco)

The plate was stored in the incubator (Heraeus) for 3-4 days at 30°C. A single colony was picked from the plate and inoculated in 150 ml baffled flask (Nalgene) containing 25 ml of BMGY medium.

BMGY or Buffered Glycerol-complex Medium

1% yeast extract

2% peptone

20 100 mM potassium phosphate (pH 6.0) (Merck)

1.34% YNB

4x10-5 % d-biotin

1% glycerol (Merck)

The culture was placed into the shaker (New Brunswick) and left to grow overnight rotating at 250 rpm at 30°C. The following day 12.5 ml of the culture was inoculated into 225 ml of BMGY medium in a 1000 ml baffled flask. In order to increase the yield of expressed AChBP a larger number of flasks were used, usually 16. The flasks were placed in the shaker and start-cultures were rotated at 250 rpm at 30°C. After two days the start-cultures were centrifuged for 15 min at 2500 rpm (Sorvall RC3B+, rotor H-6000A) at room temperature. In order to increase the cell mass for bigger protein production, cell pellets of two start-culture flasks were pooled together and resuspended in 200 ml of BMMY medium containing 1% (w/v) casamino acids.

BMMY of Buffered Methanol-complex Medium + 1% casamino acids

1% yeast extract

35 2% peptone

100 mM potassium phosphate (pH 6.0)

1.34% YNB

-56

4x10-5 % d-biotin

10

15

20

25

30

35

0.5% methanol (Merck)

1% casamino acids (Difco)

The cultures were put back into the shaker (250 mm, 30°C) and induced for the following 4 days. The concentration of methanol in the medium was kept constant by adding 1% (v/v) methanol to the cultures every 24 hours. After 4 days 100 ml of culture was harvested and the original volume of 200 ml was readjusted by adding fresh BMMY medium with 1% casamino acids. The remaining cultures were induced for another 4 days. The harvested cultures were centrifuged for 15 min at 4000 mm (Sorvall RC3B+, rotor H-6000A) and the cell pellet was discarded. The supernatant was first filtered through a 0.22 µm filter (Millipore) to remove any remaining cells and it was concentrated using a Minitan system (Waters/Millipore) with 30kDa cutoff filter (Waters/Millipore). Both the filtration and concentration and were performed at 4°C. Finally, centrifugation at 16000 rpm was done (Sorvall RC5C, rotor SS-34) in order to remove any debris left after the first two steps. The final volume of concentrated sample was ~80 ml and it was dialyzed overnight against 2 x 5 ! (20 mM Tris [pH 8.0], 150 mM NaCl and 0.02% NaN3) using 15kDa cutoff dialysis membrane (Spectra/Por) at 4°C. The dialyzed protein solution (~100 ml) was loaded onto an anion-exchange column (POROS 50 HQ, Pharmacia, column volume 8 ml). After the initial wash step of ~15 column volumes using loading buffer, a salt gradient of 30 column volumes was run from 150 mM to 1000 mM NaCl. Both solutions contained also 20 mM Tris (pH 8.0) and 0.02% NaN3. The peak of interest eluted at ~300 mM NaCl (conductivity range 16-24 mS/cm). The presence of AChBP was checked by Bio-Rad Protein Assay (Bio-Rad) and SDS-PAGE and the fractions of interested were pooled and concentrated using a Centriprep with a 30kDa cutoff membrane (Amicon). The concentrated sample (volume of 5 ml) was loaded onto a gel filtration column (Superdex 200 HR 16/60, Pharmacia, column volume 120 ml) using 20mM Tris (pH 8.0), 150 mM NaCl and 0.02% NaN3. The protein eluted starting from 60 to 71 ml with peak at ~66 ml. The final purification step of the protein was done on an anion-exchange column (MonoQ HR10/10, Pharmacia, column volume 6 ml). The protein was loaded onto the column in the same buffer as eluted from the gel filtration column. The salt gradient used for the column was the identical to the one used for the POROS 50 HQ column. The fractions in the conductivity range 25-27.5 mS/cm were pooled together and dialyzed against buffer containing 50 mM HEPES (pH 7.0) and 0.02% NaN3. The protein was concentrated up to ~20 mg/ml using a Centricon with a 30kDa cutoff membrane (Amicon). The total yield was about 2 mg purified

-57

protein per liter of expressed medium. The concentrated protein was stored at 4°C and used for crystallization experiments and biochemical characterization. N-terminal sequencing revealed the presence of EAEAYVEF residues that are part of the plC9-encoded signal sequence, before residue 2. The experimental mass was determined to be 26544 Da (MALDI), which is ~2kDa more than calculated mass based on amino-acid sequence (24649 Da). The difference is assigned to glycosylation of AChBP at position Asn66 in the mature sequence, confirmed by deglycosylation experiments with N-glycosidase F (Boehringer).

The purification of the first harvest was done separately from the full harvest. They were pooled together prior to the last purification step (anion-exchange chromatography step on MonoQ column). All above mentioned chromatography columns were mounted on an FPLC system (Pharmacia) controlled by the UNICORN system (Pharmacia). All solutions used in the FPLC system were prepared with MilliQ UF+ water, filtered through 0.22 µm filter (Millipore) and degassed.

15

20

25

30

35

10

5

EXAMPLE 6: Crystallization of the AChBP

All the crystallization experiments were done by vapor diffusion technique in a hanging drop mode using 12 well tray (Nelipak) and siliconized cover slides (Hampton Research). Trays were placed in a sandwich box (Semadeni) and stored at 19°C temperature conditioned room. The initial crystallization attempts were performed using Hampton Crystal Screen I and II (Hampton Research). Drops contained 2 µI of protein (10 mg/ml in 50 mM HEPES [pH 7.0] and 0.02% NaN₃) and 2 µl of reservoir solution. From the first screen it became clear that AChBP makes crystalline precipitate in the presence of CaCl2 salt. A more detailed screen was made which produced crystals suitable for X-ray analysis. The AChBP crystals appeared in the following conditions: 9-11% (w/v) PEG 4000 (Hampton Research), 100 mM HEPES (pH 7.0), 50-200 mM CaCl₂ x 6H₂O and 0.02% NaN₃ or or PEG MME 550 10-18% in the same conditions, with 0.3 mM ZnAcetate as additive. Depending on the batch of the protein used and the CaCl₂ concentration three different crystal forms were found: orthorhombic, tetragonal and monoclinic. Both orthorhombic and monoclinic crystal forms are frequently twinned. Orthorhombic rodlike crystals appeared immediately upon setting up the crystallization experiments (in between first few hours) under high [CaCl2]. The size of the crystals varied from 0.05x0.05x0.15 to 0.25x0.25x1.0 mm. The crystals diffract X-ray up to 3 Å resolution and show high degree of mosaicity (~05-1.2°). They have the symmetry of space group P2₁2₁2₁ with cell constants of a= 120.62Å, b=137.01Å, c=161.54Å with 2 pentamer molecules per asymmetric unit. Tetragonal crystals, squared in shape,

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-58

grew at lower $CaCl_2$ concentration, reaching 0.2x0.3x0.35 mm in size. The maximal resolution obtained was 2.7 Å with a lower mosaicity (0.5°). They belong to space group $P4_22_12$ space group with cell dimensions of a=b=141.66Å, c=120.83Å with one pentamer molecule per asymmetric unit. The exact crystallization condition for the tetragonal crystal which was used for refinement of the crystal structure: 11.5% (w/v) PEG 4000, 100 mM HEPES (pH 7.0), 150 mM CaCl₂ and 0.02% NaN₃. The third crystal form, monoclinic $P2_1$, is very similar in morphology to the orthorhombic crystals with cell dimensions of a=121.1Å, b=162.1Å, c=139.4Å, β =90.13°, containing 4 pentamers per asymmetric unit. This crystals were gave lower resolution data (~3.3Å resolution). All three crystal forms were used in the structure determination of AChBP.

The resolution limit of diffraction depended very much on the size of the crystals. And the largest crystals diffracted weakly to ~4Å resolution when exposed to a conventional rotating anode X-ray source. Therefore, the use of synchrotron radiation was critical for the structure determination. The crystals had to be cryo-protected in order to slow down the damage caused by high intensity synchrotron radiation. The cryo-protection of the AChBP crystal was done in multiple steps. The first steps included the stabilization of crystal by adding the 2 µl of mother liquor (equilibrated reservoir solution) to the drop with the crystal. After 5 minutes 3 µl of stabilizing solution was added to the drop. Normally, the stabilizing solution contained slightly higher concentrations (1-5%) of the components of the original crystallization buffer. As protectant glycerol (Merck) was added, increasing the concentration stepwise from 0% to 30% (v/v). For example, the starting solution contained 15% PEG 4000, 100 mM HEPES (pH 7.0), 150 mM CaCl₂ and 0.02% NaN₃ and the final solution contained 30% (v/v) glycerol in addition to the components just mentioned. The AChBP crystals do not tolerate drastic increase in the glycerol concentrations therefore a gentle but more time consuming approach has to be adopted. The solution around the crystal has to be stepwise exchanged (usually 5% increase of glycerol concentrations) allowing crystals to equilibrate for at least 5 minutes in each glycerol concentration. Once the crystals were equilibrated in stabilizing solution with 30% glycerol they were flash-cooled in liquid nitrogen or in the cryo-stream. In all three space groups AChBP forms a decamer structure with perfect 52 symmetry, where two pentamers contact each other through a calcium-binding site, at the 'top' of the a1 helix. This binding site (Asp2 and Asp5 from two monomers) is not conserved in the LGIC family. In the tetragonal space group the 2-fold of the a crystallographic two-fold, which leads to coincides with decamer

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-59

pseudocentrosymmetric behavior of the phases at low resolution. In solution the AChBP protein acts as pentamer.

Those of skill in the art will appreciate that the aforesaid crystallization conditions can be varied. Such variations may be used alone or in combination, and include final protein (optionally in complex with a ligand) concentrations between 1 mg/ml and 30 mg/ml; all combinations of AChPB/ligand to precipitant ratios; use of citrate concentrations between 0 mM and 200 mM; DTT concentrations between 0 mM and 10 mM; and any concentration of beta-mercaptoethanol; pH ranges between 5.5 and 9.5; PEG concentrations between 5% and 25% (w/v); PEG weights between 2000 and 8000; HEPES concentrations between 5 and 500 mM; use of TRIS or other solutions instead of HEPES, and any concentration or type of detergent; any other type of precipitating agent; any other buffer; any temperature between –50 °C and 30 °C; and crystallization of AChBP or complexes thereof by batch, liquid bridge, or dialysis method using these conditions or variations thereof.

EXAMPLE 7: Structure determination

The crystal structure was determined using the multiwave anomalous dispersion (MAD) technique on a Pb derivative, but non-crystallographic symmetry (NCS) averaging was necessary to obtain interpretable electron density. Collection of native data and heavy-atom derivatives were carried out at the synchrotron beam-lines in Grenoble (ESRF/BM14 and ID14) and Hamburg (DESY/BW7A, BW7B and X11). The AChBP orthorhombic crystal was soaked in stabilizing solution containing 5 mM trimethylleadacetate (MePb) for 5 days. Data sets were collected at four different wavelengths (0.9492Å, 0.8610Å, 0.9507Å and 0.9499Å) and data were integrated and reduced using DENZO/SCALEPACK (Otwinowski and Minor (1997) Processing of X-ray diffraction data collected in oscillation mode. In Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A. C.W. Carter and R.M. Sweet, eds. (New York: Academic Press), pp. 307-326). The program SOLVE (Terwilliger (1997) SOLVE: An automated structure solution for MAD and MIR. Edition 1.16) found 5 Pb sites which were situated on the interface between two pentamers. The Pb parameters were refined and phases calculated with SHARP (La Fortelle et al. (1997) Advances in MIR and MAD phasing: Maximum-likelihood refinement in a graphical environment, with SHARP. Proceedings of the CCP4 study weekend). Mean figure of merit (FOM) value for 4 wavelengths was 0.45. Search and optimization of 5-fold NCS operators were done using programs NCS6D and IMP (Kleywegt and Jones (1999) Software for handling macromolecular envelopes. Acta

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-60

Crystallo., D55, 941-944). 10-fold averaging using refined NCS operators in conjunction with density modification by DM (Cowtan (1994) DM: An automated procedure for phase improvement by density modification. In Joint CCP4 and ESF-EACBM Newsletter on Protein Crystallography 31, 34-38) yielded an interpretable electron density map. However, some parts of the pentamers were still not clearly defined. Therefore, a second MAD experiment was performed on the monoclinic crystals soaked in 10 mM MePb for 5 days. Data were collected for only two wavelengths, at the Pb peak (0.9479Å) and remote (0.9498Å) wavelength. The processing of the two collected data sets was done with MOSFLM (Leslie (1992) Recent changes to the MOSFLM package for processing film and image plate data. In Joint CCP4 and ESF-EACBM Newsletter on Protein Crystallography, Number 26) and data were scaled with SCALA (CCP4. The CCP4 suite: programs for protein crystallography. Acta Crystallog. D50, 760-763). 10 Pb sites were identified with Solve. The Pb parameters were refined and phases calculated with SHARP in single anomalous dispersion (SAD) mode using data collected at the Pb absorption peak The NCS operators needed for 20-fold averaging were found by NCS6D and improved with IMP. 20-fold averaging and density modification by program DM further improved electron density. The initial model tracing and sequence assignment were done based on the 20-fold averaged electron density with program O (Jones et al., 1991). However, parts of the molecules were not clearly defined. The electron density was further improved doing multi-crystal averaging with DMMULTI (Cowtan, 1994) using amplitudes of tetragonal, orthorhombic and native data sets and experimental phases of the orthorhombic and monoclinic MAD experiments. Initially missing parts became clearly defined and a complete model could be built. The initial atomic model was refined with the program CNS (Brünger et al. (1998) Acta Crystallogr. D 54, 905-921) against a maximum-likelihood target without experimental phases contribution using tetragonal native data which extend to 2.7Å resolution. Refinement included five-fold NCS restraints, an overall anisotropic B factor and bulk solvent correction. The five-fold NCS restraints were released for the parts of the pentamer that clearly do not follow the five-fold symmetry. The current model contains one pentamer of AChBP consisting of 1035 residues, 14 well-ordered solvent molecules, 5 Ca2+ ions, 5 Cl- ions and 5 Hepes molecules, well-ordered solvent molecules and 5 HEPES molecules. The following residues are not well defined in the electron density: -8-0 (part of α -mating S. cerevisiae signal sequence not native to AChBP EAEAYVEF; SEQ ID No. 21), 125-135, 155-165, 186-191 and 206-210.

10

15

WO 01/58951 PCT/EP01/01457

-61

Electron density is detectable in the ligand-binding site of AChBP. It is presumed that a HEPES molecule could account for this extra electron density based on its chemical properties. HEPES or N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid contains a quaternary ammonium ion similar to ligand such as acetylcholine (ACh) and d-tubocurarine. It has been proposed that the binding of ACh would be mediated by cation- π interaction involving N⁺ and π -systems of aromatic residues present in the binding site of nicotinic acetylcholine receptor. Without intending to be bound by theory it is suggested in accordance with the observation of the present invention that the observed HEPES molecule mimics ligand binding analogous to the binding of natural ligands like ACh in the ligand-binding site.

EXAMPLE 8: More detailed description of the structure determined in Example 7 As described in the previous example, the crystal structure of AChBP was solved using weak Pb MAD data in two crystal forms. The electron density map was improved substantially by cross-crystal averaging of three crystal forms with 20, 10 and 5 copies of the monomer in the asymmetric unit respectively (Table 3).

Table 1: Data collection statistics

	Data set	λ ₁ peak	λ ₂ remote	λ ₃ infl.	λ_1 peak	λ_2 infl.	Native
20	Space group	P2 ₁ 2 ₁ 2 ₁		P2 ₁		P4 ₂ 2 ₁ 2	
•	Resol. (Å)	3.3/3.4-3.3			3.0/3.1-3.0		2.7/2.8-2.7
	λ (Å)	0.9492	0.8610	0.9507	0.9479	0.9498	0.943
	Compl. (%)	99.7/99.7	99.6/99.6	99.7/99.7	99.9/99.9	99.5/99.5	97.8/96.5
	Mosaicity (°)	0.62	·		0.43		0.78
25	Redundancy	3.7/3.8	3.8/3.9	3.7/3.8	3.5/2.2	3.2/2.0	6.5
	R _{merge} (%)	7.7/46.8	7.8/45.2	8.3/55.0	5.9/26.1	6.0/32.9	5.9/67.4
	l/ol	8.7/1.6	8.4/1.7	8.3/1.4	7.7/2.7	6.8/1.5	27.4/2.3

			-62		
Phasing	ISO/ANO	ISO/ANO	ISO/ANO	ISO/ANO	ISO/ANO
R _{cullis} (%)	0.74/0.89	n.a./0.92	0.54/0.94	n.a./0.74	0.66/0.77
					•
Phasing power	0.57/1.2	n.a./1.06	2.3/0.91	n.a./1.1	0.37/1.22
			•		
FOM (overall)	0.45			0.28	

5

10

15

20

25

30

35

The structure was refined at 2.7 Å in space group P42212, with one AChBP pentamer in the asymmetric unit. Thus, native data (X11) were collected and the Pb-1 data sets (BW7A) at the EMBL/DESY synchrotron in Hamburg and the Pb-2 data sets (BM14) at the ESRF, Grenoble (Table 3). Data were processed with DENZO/SCALEPACK (Otwinowski & Minor, Methods Enzymol. 276, 307-326 1997) (native) or MOSFLM (Leslie, Acta Crystallogr. D. Biol. Crystallogr. 55, 1696-1702, 1999)/SCALA (CCP4) (Pb-1, Pb-2). The Pb sites, located at the interface of two pentamers, were found for both MAD sets by SOLVE (Terwilliger, Acta Crystallogr. 55, 849-861, 1999) and heavy atom parameters were optimized with SHARP (La Fortelle et al., Methods Enzymol. 276, 472-494, 1997). NCS operators were found and refined with NCS6D and IMP (Kleywegt and Jones, SERC Daresbury Laboratory, Warrington, pp. 59-66, 1994). DM-multi (Cowtan, Joint CCP4 and ESF-EACBM Newsletter on Protein Crystallography, 31, 34-38, 1994) multi-crystal averaging used amplitudes of monoclinic, orthorhombic and native (tetragonal) data sets and experimental phases of the orthorhombic and monoclinic MAD experiments. The model was built in O (Jones et al., Acta Crystallogr. A47, 110-119, 1991) and refined with the program CNS (Brünger et al., Acta Crystallogr. D54, 905-921, 1998), against the tetragonal data to 2.7 Å resolution. Refinement included partial 5-fold NCS restraints, an overall anisotropic B factor and bulk solvent correction. The unusual double cysteine Cys187-Cys188 formed a clear disulfide bridge. Because of the limited resolution it was refined with standard parameters. The final model contains 1025 residues of AChBP pentamer, 5 HEPES molecules, 10 Ca2+ ions and 15 water molecules. The entire AChBP pentamer is well ordered, except for the N-terminal 7 residues (part of the signal sequence) and the last five C-terminal residues. In addition, the HEPES, the loop region 155-160 and the sugar residues attached to residue Asn66 are not well resolved in the electron density. R.m.s deviations from ideal geometry for bond distances and angles are 0.01 Å and 1.6°, respectively. The sequence alignment was calculated by CLUSTALX (Thompson et al., Nucleic. Acids. Res. 25, 4876-4882,

-63

1997) and the corresponding figure with Espript (Gouet et al., Bioinformatics. 15, 305-308, 1999). Figures 2-5 were done using programs MOLSCRIPT (Kraulis, P.J., J. Appl. Cryst. 24, 946-950, 1991), BOBSCRIPT (Esnouf, Acta Crystallogr. D55, 938-940, 1999) and RASTER3D (Merritt and Bacon, Methods Enzymol. 277, 505-524, 1997). Refinement took place with partial five-fold NCS restraints, resulting in an R-factor of 26.4% (R_{free} = 30%).

The AChBP pentamer:

5

10

15

The AChBP homopentamer, when viewed along the five-fold axis, resembles a windmill toy, with petal-like monomers (Fig. 6a). When viewed perpendicular to the five-fold axis it has a disc-like appearance (Fig. 6b). The overall proportions of the pentamer are ~80x80x62 Å, and the diameter of the central hole is ~18 Å. These dimensions are in good agreement with the *Torpedo* nAChR N-terminal domain EM data (Miyazawa et al., J. Mol. Biol. 288, 765-786, 1999). The only subunit contacts in the AChBP pentamer are dimer interfaces, of which each monomer has two, one called the plus side and one called the minus side. We refer to the A (plus)-B (minus) interface, as example for the five equivalent interfaces AB, BC, CD, DE and EA (Fig. 6).

20 The AChBP monomer:

Each AChBP monomer is a single domain protein, asymmetric in shape, with a size of ~50x21x27 Å (Fig. 12a). It consists of an N-terminal β -helix, two short 3_{10} helices and a core of 10 β -strands forming a β -sandwich. The order of β -strands conforms to a modified immunoglobulin (Ig) topology (Fig. 12b) with an extra β -hairpin (f'-f") and an extra strand (b') (Bork et al., J. Mol. Biol. 242, 309-320, 1994). These additional strands introduce two so-called "Greek key" folding motifs. The Ig-based structure prediction (Le Novère et al., 1999; Corringer et al., Biophys. J. 76, 2329-2345, 1999) agrees well with the AChBP structure, although location of the binding site was missed due to the presence of extra β -strands (Fig. 12b). Compared to the classical Ig-fold, the AChBP β -strands are considerably twisted, with the β -sheets rotated against each other, resulting in two separate hydrophobic cores. Thus the three-dimensional fold does not resemble other Ig-like proteins and comparison to the protein database (Holm and Sander, Nucleic. Acids. Res. 25, 231-234, 1997) did not result in a significant match to any known structure.

30

10

15

20

25

WO 01/58951 PCT/EP01/01457

-64

Positioning of functional regions:

Couple of regions that are important to receptor function can be localized in the AChBP structure. In muscle type nAChRs the main immunogenic region (MIR), comprising residues α_167 - α_176 , acts as an epitope in the autoimmune disease myasthenia gravis (Tzartos et al., Mol. Neurobiol. 5, 1-29, 1991). Although the MIRrelated region in AChBP (residues 65-72) shows no sequence homology to the α₁subunit, its location in loop L3 at the top of the pentamer in a highly accessible position agrees well with the expected accessibility for this region. It also fits with EM studies that located the MIR at the distal end of the receptor relative to the membrane (Beroukhim and Unwin, Neuron 15, 323-331, 1995). On each AChBP monomer, a large cavity that is accessible from the central pore of the pentameric ring can be seen. The cavity is framed at the entrance by β-strands (β3, β4, β5 and β5') (Fig 12a) and is uncharged, mainly hydrophobic, in character. This region probably corresponds to the tunnel framed by twisted β-strands that was observed in the α_1 -subunit of *Torpedo* receptor at 4.6 Å resolution (Miyazawa et al., J. Mol. Biol. 288, 765-786, 1999). However, this cavity is not in contact with another large pocket observed at each interface between subunits. These latter pockets are lined by residues shown to be involved in ligand binding in nAChR (Arias, Neurochem. Int. 36, 595-645, 2000; Corringer et al., Annu. Rev. Pharmacol. Toxicol. 40, 431-458, 2000). They are buried from the solvent, and located close to the outside of the pentameric ring. When viewed perpendicular to the five-fold axis they are roughly equatorially positioned, ~30 Å away from the C-termini (Fig. 6b), conforming to the expected location of the Torpedo receptor ligand-binding site, as

The ligand-binding site:

30 Each ligand-binding site is found in a cleft formed by a series of loops from the principal face of one subunit and a series of β-strands from the complementary face of an adjacent subunit. It is a large cavity buried by a series of loops from the principal side and by a β-strands from the complementary side (Fig. 13). The principal side on the plus side of the AB interface consists of residues coming from 'loop A' (TyrA89), 'loop B' (TrpA143, A145) and 'loop C' (TyrA185, the double cysteine A187-A188, and TyrA192) (Fig 13c). The complementary part of this binding

determined by labeling (Fernando Valenzuela et al., Biophys. J. 66, 674-682, 1994)

and EM studies (Unwin, J. Mol. Biol. 229, 1101-1124, 1993).

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-65

site is contributed by monomer B and made of 'loop D' (TrpB53, GlnB55), 'loop E' (ArgB104, ValB106, LeuB112 and MetB114) and 'loop F' (TyrB164) (Fig 13d). In this pocket four of the aromatic residues form the bottom half of the cavity (TyrA89, TyrA185, TyrB164 and TrpB53). The pocket walls are formed by the TyrA192, TrpA143, main chain of A145 Met B114, the side-chain of GlnB55 and the double cysteine (CysA187-CysA188). The hydrophobic parts of ArgB104, ValB106 and LeuB112 form the top of the pocket (Fig 13a).

All residues in the pocket had been successfully identified by photoaffinity labeling and mutagenesis studies (Arias, Neurochem. Int. 36, 595-645, 2000; Corringer et al., Annu. Rev. Pharmacol. Toxicol. 40, 2000). Although the side chain of HisA145 is pointing away from the cavity, its main chain is involved. One residue identified by labeling studies, TrpA82 (α₁Trp86) (Galzi et al., J. Biol. Chem. 265, 10430-10437, 1990; Dennis et al., Biochemistry 27, 2346-2357, 1988) is involved in hydrophobic core formation and located far from the pocket, thus not participating in ligand binding. Otherwise, the AChBP ligand-binding site confirms the available biochemical and mutational data on nAChR completely.

The structure, however, shows for the first time how these residues are positioned with respect to each other and therefore provide a valuable tool for drug design as described in the above description of the present invention.

All observed residues are conserved between known nicotinic ligand-binding subunits except the 'loop F' TyrB164 residue. The 'loop F' region has an unusual conformation, but since it is relatively weakly resolved, its precise analysis is difficult. The 'loop F' region is stabilized in the structure by a calcium binding site formed by AspB161, AspB175 and the main chain of B176. This Ca2+ ion is structurally important for TyrB164 orientation and could therefore be important for proper ligand binding. The present findings are supported by labeling studies on muscle/Torpedo subunits showing that residues homologous to AspB161, γAsp174/δAsp180 play a role in ligand binding (Czajkowski et al., Proc. Natl. Acad. Sci. U.S.A. 90, 6285-6289, 1993; Czajkowski and Karlin, J. Biol. Chem. 270, 3160-3164, 1995; Martin et al., J. Biol. Chem. 271, 13497-13503, 1996). Additionally, calcium binding sites that enhance the response to agonist binding have been identified in the homologous region (residue range 161-172) of neuronal α₇ receptor (Galzi et al., EMBO J. 15, 5824-5832, 1996). The 'loop F' region has low sequence conservation in the nicotinic family (Fig. 11) and in other superfamily members it may well have a different conformation, even to the extent of forming a β-strand that connects the two sheets

-66

into a β -barrel. Such changes could well lead to variations in affinity, e.g. by changing the size of the ligand-binding site or its access route.

The most likely access routes to the Ilgand binding sites are from above or below the double-cysteine-containing 'loop C' (Fig. 13a). This region buries the pocket from the solvent and therefore prevents access from the outside. Access from the central pore has been suggested in the literature (Miyazawa, J. Mol. Biol. 288, 765-786, 1999), but this would require major structural rearrangements at the interface, which makes it less likely.

10

15

20

5

Ligand binding:

Surprisingly, features of bulky electron density were found that stacked onto Trp143 in each ligand-binding site in the experimental cross-crystal averaged electron density (Fig 13b). Upon consideration we have assigned this to a HEPES (N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid) buffer molecule, that contains a positively charged quaternary ammonium group and therefore has some similarity to known nicotinic receptor ligands. Its EC50 is 100 mM, indicating that its binding under crystallization conditions (100-150 mM) is possible. Although HEPES molecule does not make any specific contacts with the protein, it stacks with its quaternary ammonium onto Trp143, making cation-π interactions as expected for nicotinic agonists (Dougherty, Science 271, 163-168, 1996) (Fig. 13b). However, due to limited resolution of the present data and probable low occupancy, the precise orientation of the HEPES molecule should be taken with some degree of reservation.

It has been suggested (Changeux and Edelstein, Neuron 21, 959-980, 1998) that the ligand-binding site of nAChRs could be similar to that of acetylcholinesterase (AChE). Although the size of the binding site is roughly similar in AChBP and AChE, the observed arrangement of aromatic residues is quite different. However, the stacking of the quaternary ammonium of HEPES, as far as it has been refined in the current AChBP structure, is similar to that of the quaternary ammonium of the decamezonium in AChE on the Trp84 residue (Harel et al., Proc. Natl. Acad. Sci. U.S.A. 90, 9031-9035, 1993).

Subunit arrangement:

35 From the location of the ligand-binding site conclusions can be drawn about the relative arrangement of subunits in the *Torpedo* and muscle receptors. It has been suggested that the $\alpha_1\gamma$ and $\alpha_1\delta$ interfaces occur in a clockwise $\alpha_1\gamma\alpha_1\delta\beta_1$ arrangement

-67

when looking towards the membrane (Machold et al., Eur. J. Biochem. 234, 427-430, 1995). Such a clockwise arrangement disagrees with the structure determined in accordance with the present invention, because the relative arrangement of the principal binding site and its complementary partner is anticlockwise when looking towards the 'bottom' (membrane) side of the pentamer (Fig. 6).

Pentamer interface:

5

10

15

20

25

The subunit interface consists on the plus side entirely of loop regions (L1, L2, L4, L5, L7, L8 and L10), whereas the minus side mostly presents secondary structure elements to the interface (α1, β1, β2, β3, β5, β6 and L9) (Fig. 14). Several residues are important for both ligand-binding and pentamer formation. The interface buries a considerably surface area (2700 Å²), with a mainly uncharged character including only a single bifurcated salt bridge (GluA149-ArgB3 and ArgB104). Most intriguing about the interface residues is the lack of conservation of these particular residues in the entire superfamily, not only with AChBP, but also amongst each other (Fig. 11). These changes involve major changes in character, including changes from hydrophobic to charged. Even when a residue is conserved in any particular subunit, its expected counterpart is missing (either in the same subunit, as in the α_7 homopentamers, or in contacts such as muscle $\alpha_1\delta$ or $\alpha_1\gamma$ or neuronal $\alpha_4\beta_2$) with the sole exception of the ligand-binding site. The high level of structural conservation however, determines involvement of the same topological regions in these contacts in all family members (Fig 14b). This indicates that shape complementarity must play a major role in determining the conservation of the pentamer structure. It also indicates that different combinations of subunits will have different interfaces, creating variations in the precise allosteric contacts and movements in the various subclasses of these ion channels.

Ligand-gated ion channels:

The lack of conservation of the interface residues seems a general feature in the superfamily of LGICs, as the residues that form the interface are among the least conserved regions of the domains (Fig. 11). Apparently pentamer formation does not impose very stringent evolutionary requirements in this case. However, there is clear sequence conservation within the superfamily (Fig. 11) and it is interesting to analyze this in the light of the structure.

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-68

In the AChBP monomer structure the conserved hydrophobic residues can be grouped into three clusters (Fig. 15). In AChBP, as in other proteins with Ig-like fold, the packing of the β-sheets is promoted mainly by hydrophobic and to a lesser extent by electrostatic interactions. The first cluster is involved in packing of the N-terminal helix α1 against the main framework of the monomer and it involves residues 6, 10, 63, 65, 71, 81, 105 and 111. The second cluster, comprising residues 20, 27, 29, 31, 58, 82, 84, 86, 140, 150, 152 and 195, is situated in the upper half of the β-core region. The third cluster, including residues 33, 35, 38, 41, 48, 52, 125, 138, 171, 173, 199 and 201, is located at the lower end of the structure (Fig 15). The only nonhydrophobic residues that are highly conserved in the superfamily are Asp60, Asp85, Asn90 and Gly109. Asp60 and Gly109 are involved stabilizing the turns of a Greek key motif connecting strands β3, β5, β6 and β2, where Asp60 stabilizes the Nterminus of a small 310 helix and Gly109 enables tight turn formation. Conserved residues Asp85 and Asn90 are involved in packing of the β-sheets. Asp85 forms hydrogen bonds to the highly conserved Ser142 and Thr144 and residue Asn90 brings together the main-chain oxygens of Ser122 and Arg137, enabling disulfide bond formation of the nearby absolutely conserved disulfide bond (123-136). This disulphide bond is topologically equivalent to so-called 'tyrosine cornerstone' (Hemmingsen et al., Protein Sci. 3, 1927-1937, 1994), which links the two β-sheets together in Ig-like proteins. This explains why in the Torpedo receptor the Cys128-Cys142 bond is important for both preservation of subunit conformational stability (Mishina et al., Nature 313, 364-369, 1985) and complete nAChR assembly (Green & Wanamaker, J. Neurosci. 18, 5555-5564, 1998). Since the observed overall structural conservation is high, it is clear that all LGIC N-terminal domains will have the same three-dimensional structure.

In contrast to the above residues, the Cys-loop is a highly conserved hydrophobic region in the LGIC family but presents a totally different character in AChBP (Fig. 11).

In AChBP, this loop is hydrophilic and is found at the bottom (membrane) side of the protein, at the dimer interface. This location and its hydrophobicity in the LGIC family implies that this loop could interact with the membrane or with the transmembrane region of the receptors, functions that are absent in AChBP.

Since all ligand gated ion channels have intrinsically the same function, opening of a membrane pore, it is likely that the conserved regions of the protein determine this function. That also indicates that it is unlikely that the interface of the pentamer has a major role in opening the channel. It is possible that the conserved Cys-loop is

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-69

directly involved in transmitting this kind of information to the membrane part of the LGICs. Another option is that large structural changes in the β -sheet regions play a role in opening the channel. Indeed, the movement observed at 9 Å for *Torpedo* nAChR upon agonist binding (Unwin, Nature 373, 37-43, 1995), fits well with such a suggestion. In accordance with the present invention a twisted β -sandwich would be observed, with two distinct hydrophobic cores and it is entirely possible that these cores move with respect to each other upon ligand binding. The effect of such movements will then be modulated by the varying subunit interfaces in the different subtypes of the receptor, allowing intricate specificity in the neuronal signal transmission.

EXAMPLE 9: Ligand-binding crystallization studies

AChBP was cocrystallized in complex with α-bungarotoxin (αBTX, Sigma). Prior to the crystallization experiments the stability of the complex has been investigated. Using gel-filtration chromatography (Superdex 200 HR 10/30, Pharmacia, column volume 24 ml) it has been found that it is possible to purify stable complex between AChBP and αBTX. The gel-filtration run was performed using 20 mM Tris (pH 8.0), 150 mM NaCl and 0.02% NaN3. The stability of the complex was also confirmed with native PAGE. The crystallization experiments were done based on the same set of conditions found to work for AChBP alone; see Example 6. A small screen was set precipitant concentrations and various AChBP:α BTX with different concentrations. Tiny crystals appeared in the conditions containing 10-12% PEG 4000, 100 mM HEPES (pH 7.0), 20-80 mM CaCl₂ and 0.02% NaN₃. The best looking crystals grew under above mentioned conditions when AChBP: (BTX were mixed in 1:10 molar ratio. In order to check if complex indeed crystallized, crystals were thoroughly washed, dissolved in denaturing buffer and checked on SDS-PAGE that clearly showed that they contained both proteins.

In addition, a number of small ligands were bound to AChBP in soaking experiments. These include: B-bippinatin (a synthetic analog of lophotoxin), acetylcholine (ACh, Slgma), d-tubocurarine chloride (Sigma), carbamylcholine chloride (CCh, Sigma), galanthamine hydrobromide (Sigma), epibatidine (Sigma) and nicotine (Sigma). The soaking solutions were made of stabilizing solutions (see Example 6) and together with dissolved ligands (ligands were normally dissolved in 20 mM HEPES [pH 7.0]). The ligand concentrations used were dependent on its binding constants, as determined by ligand-binding studies. The soaking times were different depending on the ligand used. After the soaking step the crystals were flash-cooled in liquid nitrogen.

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-70

EXAMPLE 10: Generating human alpha7 nAChR / AChBP chimeras

The chimeric proteins of nAChR subunits and AChBP can be used as tools in the development of novel, nAChR subtype specific ligands. As a first step in developing these tools chimeric proteins have been designed and constructed in which part(s) of the human alpha7 nAChR were grafted into AChBP. Previous studies on the molecular determinants of ligand-binding by the alpha7 nAChR have identified three amino acid domains that compose the primary part of the ligand-binding site, further referred to as "loops A, B, and C". Within each of the three loops amino acid residues are present that are thought to directly interact with the ligand. Based on sequence conservation of the nAChR and AChBP the three possible ligand-binding loops of AChBP have been pin-pointed in accordance with the present invention as follows: loop A, Trp-101 -> Tyr-108; loop B, Trp-162 -> His-164; loop C, Tyr-204 -> Tyr-211. The chimeric proteins that were constructed replace either one (A, B or C) or multiple (A&B, A&C, B&C and A&B&C) of the ligand-binding loops of AChBP with the corresponding human alpha7 nAChR sequence.

The loop-A domain of AChBP was replaced by the corresponding domain of the human alpha7 nAChR using a two-step polymerase chain reaction (PCR). In the first step two separate PCR amplifications (35 cycles: 94 °C;30 sec., 58 °C; 30 sec and 72 °C; 60 sec.) yielded two halves of the chimera construct. AChBP cDNA (wild type) was used as template, and outer primers located either just before the start codon (gcgctcgagaaaagagaggctgaagctttggaccgggcagacatctt; SEQ ID No. 17) or just before the stop codon (cgcgaattcaagaatttcggagcgtccctt; SEQ ID No. 18) were each used in combination with two internal primers gtggaaaccagacattctcctctacaacgccatctcgaaacc (SEQ ID No. 19) and gaggagaatgtctggtttccacaaagagcttattggcac (SEQ ID No. 20), respectively. The internal primers contained a 5'-tag-sequence that encoded for the introduced alpha7 nAChR domain. As such the two generated chimeric PCR products share a common tag containing a part of the alpha7 nAChR subunit. In the second step, the two PCR products from the first round were pooled and, in the absence of primers, went through 5 rounds of PCR amplification (94 9C; 30 sec., 54 ²C; 3 mm. and 72 ²C; 90 sec.). This allowed the two halves of the chimera to anneal to each other at the common alpha7 nAChR tag. The subsequent addition of the two outer primers and another 35 cycles of 25 PCR amplification (94 °C; 30 sec., 58 °C; 30 sec. and 72 °C; 90 sec.) yielded the final chimera construct. All PCR amplifications were hot-started and performed using PFU DNA-polymerase (Invitrogen). The loop-A AChBP/alpha7 chimera was cloned, using Xhol/EcoRI restriction sites in the outer primers, into the His-tag containing yeast expression

25

WO 01/58951 PCT/EP01/01457

-71

vector pPIC9 (Invitrogen). Validation of the construct was achieved by DNA sequencing. Expression of the chimera construct was achieved according to the Pichla pastoris protein expression protocol of Invitrogen.

As described in the examples and the description, the present invention provides water-soluble ligand-binding proteins derived from molluscs and analogs of ligand-gated ion channels, crystals thereof and their use for screening ligands of ligand-gated ion channels. In particular, ligand-binding proteins have been identified that are capable of forming multimers and are amenable to crystallization. The crystall structure of one these proteins, an acetylcholine binding protein (AChBP) is provided, which can be used to generate 3D models of the extracellular ligand-binding domain of ligand-gated ion channels and thus for screening of drugs that act on these ion channels. Furthermore, chimeric proteins are provided that are capable of binding a ligand of a ligand-gated receptor, and comprising at least the amino acids of the AChBP determining solubility of the AChBP, in the same positions as in the AChBP, and furthermore comprising amino acids determining binding to said ligand.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Description, and Examples is hereby incorporated herein by reference. Moreover, the sequence listing is herein incorporated by reference.

PCT/EP01/01457

-72 **Table 1**

			_			sion 7.0						
_	CRYST1	141.		141.					90.00			
5	ORIGX1		1.000			.000000	0.00000		0.00000			•
	ORIGX2		0.000	000	1	.000000	0.00000		0.00000			
	ORIGX3		0.000	000	0	.000000	1.00000	0	0.00000			
	SCALE1		0.007	059	0	.000000	0.00000	0	0.00000			
	SCALE2		0.000	000	0	.007059	0.00000	0	0.00000			
10	SCALE3		0.000	000	0	.000000	0.00827	3	0.00000			
	ATOM	1	CB	PHE	Α	1	65.468	25.127	1.161	1.00	73.24	6
	MOTA	2	CG	PHE	Α	1	64.224	24.803	0.370	1.00	76.49	6
	ATOM	3		PHE		1	63.433	25.819	-0.178	1.00	77.52	6
	ATOM	4		PHE		1	63.798	23.471	0.244		78.15	6
15	ATOM	5		PHE		1	62.224	25.522	-0.840		79.11	Ĝ
. •	ATOM	6		PHE		1	62.590	23.148	-0.412		79.82	6
	MOTA	7	CZ	PHE		1	61.797	24.179	-0.958		79.89	6
	ATOM	8	C	PHE		1	66.638	27.146	1.923		69.89	6
	ATOM	9	0	PHE		1	67.034	26.519	2.903		70.26	8
20				PHE		1	67.407	25.990	-0.118		71.31	7
20	ATOM	10	N			1		26.375	0.689		70.93	6
	ATOM	11	CA	PHE			66.214		1.909		68.78	7
	ATOM	12	N	ASP		2	66.562	28.478				6
	MOTA	13	CA	ASP		2	66.958	29.233	3.105		68.57	
OF	MOTA	14	CB	ASP		2	67.577	30.615	2.739		69.98	6
25	ATOM	15	CG	ASP		2	66.639	31.523	1.914		73.55	6
	ATOM	16		ASP		2	67.059	32.068	0.844		73.75	8
	MOTA	17		ASP		2	65.485	31.714	2.349		75.27	8
	MOTA	18	С	ASP		2	65.794	29.374	4.102		67.66	6
00	MOTA	19	0	ASP		2	64.622	29.273	3.719		68.25	8
30	MOTA	20	N	ARG		3	66.126	29.560	5.386		65.60	7
	MOTA	21	CA	ARG		3	65.131	29.703	6.453		60.77	6
	MOTA	22	CB	ARG		3 .	65.765	30.222	7.737		60.30	6
	MOTA	23	CG	ARG		3	66.393	29.174	8.604		59.51	6
	MOTA	24	CD	ARG		3	66.375	29.629	10.048		61.41	6
35	MOTA	25	NE	ARĢ		3	66.440	28.471	10.927		61.03	7
	ATOM	26	cz	ARG	Α	3	67.550	27.787	11.159		62.03	б
	MOTA	27	NH1	ARG	Α	3	68.692	28.169	10.586		60.01	7
	MOTA	28	NH2	ARG	Α	3	67.509	26.694	11.918	1.00	62.76	7
	MOTA	29	C	ARG	Α	3	64.034	30.659	6.055		59.92	6
40	ATOM .	30	0	ARG	Α	3	62.883	30.487	6.454		59.64	8
	MOTA	31	N	ALA	Α	4	64.395	31.685	5.291		57.25	7
	ATOM	32	CA	ALA	Α	4	63.404	32.641	4.836	1.00	55.16	6
	ATOM	33	CB	ALA	Α	4	64.065	33.782	4.088	1.00	53.78	6
	ATOM	34	C	ALA	Α	4	62.421	31.917	3.927	1.00	54.69	6
45	ATOM	35	0	ALA	Α	4	61.213	32.062	4.074	1.00	55.60	8
	MOTA	36	N	ASP	Α	5	62.942	31.127	2.995	1.00	54.79	7
	ATOM	37	CA	ASP		5	62.097	30.392	2.060	1.00	55.84	б
	ATOM	38	CB	ASP		5	62.937	29.580	1.058	1.00	56.83	6
	MOTA	39	CG	ASP		5	63.918	30.437	0.278		59.97	6
50	ATOM	40		ASP		5	63.519	31.519	-0.213	1.00	61.60	8
	MOTA	41		ASP		5	65.095	30.025	0.148	1.00	62.19	8
	ATOM	42	C	ASP		5	61.176	29.443	2.815		55.90	6
	ATOM	43	Ö	ASP		5	60.011	29.268	2.445		53.57	8
•	MOTA	44	N	ILE		6	61.695	28.832	3.877		55.26	7
55	ATOM	45	CA	ILE		6	60.890	27.889	4.650		55.12	6
55	ATOM	46		ILE		6	61.743	27.107	5.657		55.82	6
	ATOM	47		ILE		6	60.878	26.056	6.354		53.18	6
	ATOM	48		ILE		6	62.924	26.455	4.933		56.24	· 6
	ATOM	49		ILE		6	63.802	25.568	5.816		59.65	6
60	ATOM	50		ILE		6	59.742	28.561	5.396		54.71	6
00	ATOM	50	_	TILL	n	J	33.144	20.501	٥٠٥٠	00	J=. / L	U

	WO 01/58951									PCT/EP01/014	157
							-73				
			_		_	_		00 150		4 00 55 55	_
	MOTA	51	0	ILE		6	58.589	28.159	5.256	1.00 55.75	8
•	ATOM	52	N	LEU		7	60.058	29.583 30.299	6.182	1.00 52.58	7
	ATOM ATOM	53	CA	LEU		7 7	59.041 59.697		6.929	1.00 51.88 1.00 51.65	6
5		54	CB	LEU			=	31.387	7.784		6
J	ATOM ATOM	55 56	CG CD1	LEU		7 7	60.589 61.484	30.828 31.902	8.895 9.480	1.00 51.59 1.00 51.45	· 6
	ATOM	57		LEU		7	59.700	30.225	9.953	1.00 51.45	6
	ATOM	58		LEU		7	58.048	30.223	5.961	1.00 51.32	6
	ATOM	59	0	LEU		7	56.846	30.921	6.204	1.00 51.40	8
10	ATOM	60	N	TYR		8	58.561	31.417	4.848	1.00 51.83	7
. •	ATOM	61	CA	TYR		8	57.727	32.041	3.832	1.00 53.61	6
	ATOM	62	CB	TYR		8	58.601	32.520	2.672	1.00 55.43	6
	ATOM	63	CG	TYR		8	57.806	33.119	1.543	1.00 57.65	6
	ATOM	64		TYR		8	57.217	34.379	1.668	1.00 58.24	6
15	ATOM	65		TYR		8	56.439	34.914	0.644	1.00 58.94	6
	ATOM	66	CD2	TYR		8	57.601	32.407	0.366	1.00 58.93	6
	ATOM	67	CE2	TYR	Α	8	56.825	32.930	-0.665	1.00 60.13	6
	ATOM	68	CZ	TYR	Α	8	56.244	34.183	-0.518	1.00 60.03	6
	ATOM	69	OH	TYR	Α	8	55.453	34.699	-1.527	1.00 63.97	8
20	ATOM	70	С	TYR	Α	8	56.636	31.114	3.296	1.00 52.67	6
	ATOM	71	0	TYR	Α	8	55.483	31.511	3.143	1.00 52.13	8
	ATOM	72	N	ASN	Α	9	57.009	29.880	2.997	1.00 53.39	7
	ATOM	73	·CA	ASN		9	56.051	28.918	2.488	1.00 53.87	6
~-	ATOM	74	CB	ASN		9	56.750	27.613	2.096	1.00 58.21	6
25	ATOM	75	CG	ASN		9	57.646	27.772	0.860	1.00 62.45	6
	ATOM	76		ASN		9	57.647	28.824	0.209	1.00 64.72	8
	ATOM	77		ASN		9	58.405	26.724	0.530	1.00 62.99	7
	MOTA	78	C	ASN		9	54.987	28.638	3.526	1.00 53.31	6
20	ATOM	79	0	ASN		9	53.794	28.725	3.239	1.00 52.02	8
30	ATOM	80	N	ILE		10	55.420	28.300	4.736	1.00 53.77	7
	ATOM	81	CA	ILE		10	54.489	28.018	5.829	1.00 55.18	6
	ATOM	82	CB	ILE		10	55.229	27.788	7.150	1.00 53.51	6
	ATOM	83		ILE		10 10	54.220	27.639	8.272	1.00 53.99	6
35	ATOM ATOM	84 85		ILE		10	56.109 57.043	26.541 26.346	7.044 8.202	1.00 50.48 1.00 47.68	6 6
00	ATOM	86	CDI	ILE		10	53.523	29.183	6.032	1.00 47.08	6
	ATOM	87	o	ILE		10	52.319	28.997	6.221	1.00 57.42	8
	ATOM	88	N	ARG		11	54.070	30.390	5.997	1.00 58.29	7
	ATOM	89	CA	ARG		11	53.283	31.600	6.156	1.00 60.48	6
40	ATOM	90	CB	ARG		11	54.199	32.810	6.042	1.00 64.72	6
· .	ATOM	91	CG	ARG			53.513	34.134		1.00 70.99	6
	ATOM	92	CD	ARG	Α	11	53.241	34.337	7.757	1.00 79.75	6
	ATOM	93	NE	ARG	Α	11	53.059	35.751	8.105	1.00 86.33	7
	ATOM	94	CZ	ARG	A	11	53.848	36.733	7.665	1.00 89.85	6
45	ATOM	95	NH1	ARG	Α	11	54.871	36.451	6.845	1.00 92.68	7
	ATOM	96	NH2	ARG	A	11	53.636	37.992	8.056	1.00 90.02	7
	ATOM	97	С	ARG		11	52.204	31.701	5.082	1.00 59.54	6
	ATOM	98.	0	ARG		11	51.038	31.954	5.363	1.00 59.64	8
	ATOM	99	N	GLN		12	52.614	31.489	3.841	1.00 59.22	7
50	ATOM	100		GLN		12	51.718	31.595	2.705	1.00 58.15	6
	MOTA	101	CB	GLN		12	52.542	31.776	1.441	1.00 59.05	6
	ATOM	102	CG	GLN		12	52.118	32.961	0.629	1.00 60.64	6
	ATOM	103	CD	GLN		12	52.674	34.226	1.192	1.00 61.53	6
55	ATOM	104		GLN		12	53.879	34.345	1.360	1.00 65.50	8
55	ATOM	105		GLN		12	51.811 ·	35.182	1.489	1.00 62.18	7
	MOTA MOTA	106	C	GLN GLN		12 12	50.732	30.460	2.472	1.00 57.30	6
	ATOM	107 108	N	THR		13	49.714 51.029	30.651 29.280	1.814 2.987	1.00 57.03 1.00 56.84	8 7
	ATOM	109	CA	THR		13	50.142	28.147	2.773	1.00 57.26	6
60	ATOM	110	CB	THR		13	50.922	26.964	2.773	1.00 57.28	6
	ATOM	111		THR		13	52.000	26.616	3.071	1.00 55.40	8
						_				•	

	WO 01/58	951								PCT/EP01/0	1457
	•						-74				
	ATOM	112	CG2	THR .	A :	13	51.477	27.326	0.813	1.00 58.15	6
	MOTA	113	C	THR .	Α.	13	49.411	27.650	4.013	1.00 58.45	6
	ATOM	114	0	THR .	A :	13	48.423	26.932	3.905	1.00 58.36	8
	MOTA	115	N	SER	A :	14	49.892	28.034	5.187	1.00 60.01	7
5	MOTA	116	CA	SER .		14	49.290	27.584	6.424	1.00 60.03	6
	MOTA	117	CB	SER		14	50.198	27.930	7:601	1.00 61.46	· 6
	MOTA	118	OG	SER		14	49.813	27.207	8.758	1.00 65.18	8
	MOTA	119	C	SER		14	47.899	28.147	6.664	1.00 59.50 1.00 58.72	6 8
10	MOTA	120	0	SER		14 15	47.560 47.102	29.240 27.377	6.189 7.407	1.00 58.72	7
10	MOTA MOTA	121 122	N CA	ARG ARG		15 15	45.740	27.753	7.755	1.00 55.62	6
	ATOM	123	CB	ARG		15	44.744	26.996	6.877	1.00 56.74	6
	ATOM	124	CG	ARG		15	44.925	27.253	5.385	1.00 59.62	6
	ATOM	125	CD	ARG		15	43.688	26.851	4.614	1.00 61.99	6
15	ATOM	126	NE	ARG		15	42.519	27.540	5.151	1.00 64.02	· 7
-	ATOM	127	CZ	ARG		15	41.261	27.216	4.870	1.00 65.48	6
	ATOM	128	NH1	ARG	A	15	41.007	26.201	4.050	1.00 67.33	7
	ATOM	129	NH2	ARG	A	15	40.256	27.908	5.408	1.00 64.23	7
	ATOM	130	С	ARG	Α	15	45.516	27.420	9.219	1.00 52.12	6
20	ATOM	131	0	ARG		15	45.135	26.310	9.562	1.00 53.25	8
	MOTA	132	N	PRO		16	45.751	28.392	10.104	1.00 50.04	7
	MOTA	133	CD	PRO		16	46.198	29.750	9.773	1.00 48.52	6
	ATOM	134	CA	PRO		16	45.597	28.249	11.551	1.00 49.56	
05	MOTA	135	CB	PRO		16	45.959	29.634	12.073	1.00 49.66	6
25	MOTA	136	CG	PRO		16	46.870	30.165	11.041	1.00 49.57 1.00 50.11	6 6
	MOTA	137	C	PRO		16 16	44.215 44.060	27.816 27.322	12.016 13.131	1.00 50.11	8
	ATOM ATOM	138 139	N O	PRO ASP		17	43.208	28.013	11.176	1.00 51.27	7
	ATOM	140	CA	ASP		17	41.856	27.640	11.548	1.00 50.70	6
30	ATOM	141	CB	ASP		17	40.850	28.609	10.931	1.00 54.16	6
00	ATOM	142	CG	ASP		17	40.873	29.974	11.592	1.00 59.76	6
	MOTA	143		ASP		17	41.245	30.060	12.791	1.00 60.67	8
	ATOM	144		ASP		17	40.500	30.965	10.920	1.00 62.99	8
	ATOM	145	С	ASP	Α	17	41.482	26.218	11.157	1.00 50.71	6
35	ATOM	146	0	ASP	Α	17	40.353	25.783	11.390	1.00 48.36	8
	MOTA	147	N	VAL		18	42.429	25.484	10.583	1.00 51.85	7
	MOTA	148	CA	VAL		18	42.143	24.128	10.148	1.00 52.53	6
	MOTA	149	CB	VAL		18	42.262	24.011	8.622	1.00 53.05	6
40	MOTA	150		VAL		18	41.834	22.618	8.169	1.00 51.38	6
40	MOTA.	151		VAL		18	41.396	25.077	7.963	1.00 51.76 1.00 52.56	6
	MOTA	152	C	VAL		18	42.993 44.199	23.050 23.006	10.779 10.588	1.00 52.56	6 8
	MOTA MOTA	153 154	O N	VAL ILE		18 19	42.327	22.172	11.519	1.00 52.04	7
	ATOM	155	CA	ILE		19	42.954	21.042	12.202	1.00 52.70	6
45	ATOM	156	CB	ILE		19	41.871	20.319	13.072	1.00 52.71	6
. •	ATOM	157	CG2			19	40.819	19.671	12.190	1.00 52.40	6
	ATOM	158		ILE		19	42.504	19.290	13.992	1.00 53.50	6
	ATOM	159		ILE		19	41.546	18.811	15.056	1.00 50.39	6
	ATOM	160	C	ILE		19	43.596	20.097	11.164	1.00 52.96	6
50	MOTA	161	0	ILE	Α	19	42.957	19.687	10.193	1.00 51.39	8
	ATOM	162	N	PRO		20	44.878	19.757	11.355	1.00 53.70	7
	MOTA	163	CD	PRO		20	45.711	20.210	12.472	1.00 54.14	6
	ATOM	164	CA	PRO		20	45.644	18.876	10.461	1.00 56.34	6
E E	ATOM	165	CB	PRO		20		18.996	10.981	1.00 56.60	6
55	MOTA	166	CG	PRO		20	47.060 45.177	20.235 17.432	11.840 10.474	1.00 58.05 1.00 58.61	6 6
	MOTA	167 168	C	PRO PRO		20 20	45.177 45.974	16.523	10.474	1.00 59.22	8
	ATOM ATOM	169	N O	THR		21	43.886	17.231	10.882	1.00 59.22	7
	ATOM	170	CA	THR		21	43.283	15.900	10.236	1.00 66.91	6
60	ATOM	171	CB	THR		21	41.765	16.020	10.495	1.00 65.83	6
	ATOM	172	OG1			21	41.516	15.813	11.883	1.00 67.19	8

WO 01/58951									PCT/E	P01/01	457	
							75					
			~~~		_	0.1	-75	15 010	0 607	1 00 6	0 40	į
	ATOM	173		THR		21	40.975 43.522	15.010 15.060	9.687 8.967	1.00 6		6 6
	MOTA	174	С	THR THR		21 21	43.365	15.538	7.832	1.00 7		8
	MOTA	175	0	GLN		22	43.899	13.802	9.179	1.00 7		7
5	MOTA	176	N			22	44.152	12.844	8.096	1.00 7		6
Ç	MOTA	177 178	CA CB	GLN GLN		22	45.513	12.180	8.296	1.00 7		· 6
	MOTA					22	46.668	13.174	8.402	1.00 8		6
	ATOM ATOM	179 180	CG CD	GLN GLN		22	47.836	12.640	9.244	1.00 8		6
•	ATOM	181		GLN		22	47.709	12.451	10.467	1.00 8		8
10	ATOM	182		GLN		22	48.976	12.397	8.592	1.00 8		7
10	ATOM	183	C	GLN		22	43.055	11.779	8.158	1.00 8		6
	ATOM	184	Ö	GLN		22	43.050	10.929	9.058	1.00 8		8
	ATOM	185	N	ARG		23	42.133	11.825	7.199	1.00 8		7
	ATOM	186	CA	ARG		23	40.999	10.896	7.162	1.00 8		6
15	ATOM	187	CB	ARG		23	41.478	9.447	7.095	1.00 8		6
. •	ATOM	188	CG	ARG		23	41.983	9.032	5.717	1.00 8		6
	ATOM	189	CD	ARG		23	43.517	8.991	5.617	1.00 9		6
	ATOM	190	NE	ARG		23	43.958	8.775	4.231	1.00 9		7
	ATOM	191	CZ	ARG		23	43.557	7.768	3.447	1.00 9	4.10	6
20	ATOM	192		ARG		23	42.700	6.854	3.901	1.00 9		7
	ATOM	193	NH2	ARG	A	23	44.000	7.687	2.195	1.00 9	3.77	7
	ATOM	194	С	ARG	Α	23	40.130	11.099	8.399	1.00 8	5.22	6
	MOTA	195	0	ARG	Α	23	39.979	12.237	8.881	1.00 8		8
	MOTA	196	N	ASP	Α	24	39.549	10.011	8.908	1.00 8	6.21	7
25	ATOM	197	CA	ASP	Α	24	38.705	10.105	10.105	1.00 8		6
	MOTA	198	CB	ASP	Α	24	37.689	8.952	10.194	1.00 8		6
	MOTA	199	CG	ASP	Α	24	37.418	8.289	8.847	1.00 9		6
	MOTA	200		ASP		24	36.945	8.994	7.900	1.00 9		8
	MOTA	201	OD2	ASP	Α	24	37.680	7.058	8.756	1.00 9		8
30	MOTA	202	С	ASP		24	39.631	10.021	11.305	1.00 8		6
	ATOM	203	0	ASP		24	39.173	9.975	12,458	1.00 8		8
	ATOM	204	N	ARG		25	40.935	9.981	11.029	1.00 8		7
	MOTA	205	CA	ARG		25	41.936	9.898	12.091	1.00 7		6
05	ATOM	206	CB	ARG		25	43.309	9.539	11.527	1.00 8		6
35	ATOM	207	CG	ARG		25	43.471	8.100	11.087	1.00 8		6
	ATOM	208	CD	ARG		25	44.960	7.785	10.851	1.00 9		6
	ATOM	209	NE	ARG		25	45.187	6.380	10.489	1.00 9		7 6
	ATOM	210	CZ	ARG		25	46.388	5.815	10.345	1.00 9 1.00 9		7
40	ATOM	211 212		ARG ARG		25 25	47.495 46.487	6.537 4.522	10.530	1.00 9		7
40	MOTA		C	ARG		25	42.059					6
	ATOM ATOM	213	o	ARG		25	42.158	12.283	12.281	1.00 7		8
	ATOM	215	N	PRO		26	42.034		14.212	1.00 7		7
	ATOM	216	CD	PRO		26	41.636	9.933	14.999	1.00 6		6
45	ATOM	217	CA	PRO		26	42.152	12.281	15.083	1.00 6		6
	ATOM	218	CB	PRO		26	41.802	11.723	16.460	1.00 6		6
	ATOM	219	CG	PRO		26	40.930		16.158	1.00 6		6
	ATOM	220	Ċ	PRO		26	43.593	12.762	15.053	1.00 6	4.53	6
	ATOM	221	Ö	PRO		26	44.491		14.694	1.00 6		8
50	ATOM	222	N	VAL		27	43.816		15.420	1.00 6		7
	ATOM	223	CA	VAL		27	45.168		15.476	1.00 5	7.20	6
	ATOM	224	СВ	VAL	Α	27	45.197	16.079	15.374	1.00 5	6.96	6
	ATOM	225	CG1	VAL	Α	27	.46.535		15.872	1.00 5		6
	MOTA	226	CG2	VAL	A	27	44.986		13.930	1.00 5		6
55	MOTA	227	С	VAL	Α	27	45.685		16.835	1.00 5		6
	ATOM	228	0	VAL		27	45.026		17.849	1.00 5		8
	ATOM	229		ALA		28	46.852		16.858	1.00 5		7
	MOTA	230	CA	ALA		28	47.405			1.00 5		6
00	ATOM	231	CB	ALA		28	48.250		17.907	1.00 5		6
60	ATOM	232	С	ALA		28	48.230		18.761	1.00 5		6
	ATOM	233	0	ALA	A	28	49.324	14.451	18.294	1.00 5	2.33	8.

PCT/EP01/01457

	WO 01/583	951									PCI	/FL01/01	45/
								-76				•	
	ATOM	234	N	VAL	Δ	29		47.683	14.672	19.837	1 00	51.33	7
	ATOM	235	CA	VAL		29		48.332	15.730	20.590		49.28	6
	ATOM	236	CB	VAL		29		47.367	16.921	20.845		47.59	6
	ATOM	237		VAL		29		48.056	17.985	21.676		44.30	6
5	ATOM	238		VAL		29		46.891	17.497	19.527		44.21	6
	ATOM	239	C	VAL		29		48.782	15.171	21.930		49.54	· 6
	ATOM	240	0	VAL		29		48.014	14.524	22.635		49.14	8
	ATOM	241	N	SER		30		50.043	15.402	22.261		49.54	7
	ATOM	242	CA	SER	A	30		50.574	14.946	23.523	1.00	52.38	6
10	ATOM	243	CB	SER	Α	30		51.869	14.163	23.309	1.00	51.50	6
	ATOM	244	OG	SER	Α	30		52.846	14.945	22.645	1.00	56.10	8
	ATOM	245	С	SER	Α	30		50.819	16.187	24.362	1.00	54.25	6
	ATOM	246	0	SER	Α	30		51.360	17.174	23.880	1.00	56.41	8
	ATOM	247	N	VAL	Α	31		50.396	16.134	25.618	1.00	56.86	7
15	ATOM	248	CA	VAL	Α	31		50.543	17.258	26.531		58.42	6
	MOTA	249	CB	VAL		31		49.170	17.768	27.012		58.48	. 6
	ATOM	250		VAT		31		49.338	19.086	27.744		59.95	6
	ATOM	251		VAL		31		48.219	17.910	25.835		56.73	6
00	ATOM	252	С	VAL		31		51.328	16.803	27.747		59.56	6
20	ATOM	253	0	VAL		31		51.073	15.729	28.281		60.85	8
	MOTA	254	N	SER		32		52.271	17.631	28.185		61.06	7
	ATOM	255	CA	SER		32		53.105	17.312	29.338		60.16	6
•	MOTA	256	CB	SER		32		54.388	16.619	28.868		59.88	6
25	MOTA	257	OG	SER SER		32		55.294	16.430	29.937		60.41	8
25	MOTA ATOM	258 259	C 0	SER		32 32		53.465	18.568	30.116		60.19 61.87	6
	MOTA	260	N	LEU		33		54.206 52.946	19.416 18.689	29.621 31.333		58.89	8 7
	ATOM	261	CA	LEU		33		53.256	19.847	32.170		57.23	6
	ATOM	262	CB	LEU		33		52.112	20.142	33.142		55.20	6
30	ATOM	263	CG	LEU		33		50.740	20.363	32.511		54.66	6
••	ATOM	264		LEU		33		49.762	20.880	33.543		51.01	6
	ATOM	265		LEU		33		50.880	21.342	31.373		55.39	6
	ATOM	266	C	LEU		33		54.518	19.601	32.979		56.76	6
	ATOM	267	0	LEU		33		54.697	18.526	33.533		58.14	8
35	ATOM	268	N	LYS	Α	34		55.394	20.597	33.028	1.00	57.17	7
	ATOM	269	CA	LYS	Α	34		56.633	20.512	33.800	1.00	57.46	6
	MOTA	270	CB	LYS	Α	34		57.865	20.690	32.910	1.00	60.89	6
	MOTA	271	CG	LYS	Α	34		57.940	19.723	31.738		68.80	6
4.0	MOTA	272	$^{\rm CD}$	LYS		34		58.048	18.249	32.186		73.30	6
40	MOTA	273	CE	LYS		34		58.071	17.290	30.961		74.90	6
	ATOM	274	NZ	LYS		34	•	58.210	15.842	31.340		75.55	7
	ATOM	275	С	LYS		34		56.522	21.691	34.741		54.81	6
	ATOM	276	0	LYS		34		56.567	22.834	34.308		55.33	8
45	MOTA	277	N	PHE		35		56.358	21.422	36.026		52.88	7
45	MOTA	278	CA	PHE		35		56.215	22.507	36.976		50.00	6
	ATOM	279	CB	PHE		35		55.586	21.993 21.542	38.260		45.71 45.07	6
	MOTA ATOM	280 281	CG CD1	PHE PHE		35 35		54.186 53.912	20.256	38.072 37.634		45.46	6 . 6
	ATOM	282		PHE		35		53.133	22.429	38.252		47.46	. 6
50	ATOM	283		PHE		35		52.612	19.848	37.372		45.03	6
•	ATOM	284		PHE		35		51.819	22.036	37.990		49.48	6
	ATOM	285	CZ	PHE		35		51.560	20.735	37.547		48.14	6
	MOTA	286	C	PHE		35		57.494	23.268	37.247		49.05	6
	ATOM	287	0	PHE		35		58.549	22.687	37.480		48.49	8
55	MOTA	288	N	ILE	Α	36		57.374	24.588	37.191	1.00	46.86	7
	MOTA	289	CA	ILE	A	36		58.492	25.482	37.393	1.00	45.55	6
	MOTA	290	CB	ILE		36	•	58.538	26.551	36.284		43.92	6
	MOTA	291		ILE		36		59.771	27.411	36.433		39.03	6
00	MOTA	292		ILE		36		58.526	25.876	34.917		44.17	6
60	ATOM	293		ILE		36		59.671	24.916	34.699		46.33	6
	ATOM	294	С	ILE	Α	36		58.392	26.181	38.739	1.00	46.38	6

	WO 01/589	51								PCT	/E <b>P</b> 01/01	457
							-77					
	ATOM ATOM	295	0	ILE		36	59.405	26.580	39.318		45.40	8
	ATOM	296 297	N CA	ASN ASN		37 37	57.176 57.023	26.340	39.244		46.13	7
	ATOM	298	CB	ASN		37	57.491	27.008 28.462	40.526 40.400		46.27 46.32	6 6
5	MOTA	299	CG	ASN		37	58.009	29.030	41.707		48.59	6
	MOTA	300		ASN		37	57.408	28.844	42.759		49.38	8
	MOTA	301		ASN		37	59.124	29.743	41.639		46.71	7
	MOTA	302	С	ASN		37	55.595	26.975	41.046	1.00	46.17	6
10	ATOM	303	0	ASN		37	54.644	26.799	40.281		44.02	8
10	ATOM	304	N	ILE		38	55.465	27.117	42.362		46.64	7
	ATOM ATOM	305 306	CA CB	ILE		38	54.173	27.158	43.033		48.46	6
	ATOM	307	CG2			38 38	53.988 52.680	25.951 26.066	43.923 44.671		47.34 49.13	6
	ATOM	308	CG1			38	53.983	24.697	43.050		48.40	6 6
15	ATOM	309	CD1			38	54.079	23.402	43.791		47.55	6
	ATOM	310	С	ILE	Α	38	54.245	28.433	43.847		50.74	6
	ATOM	311	0	ILE		38	54.979	28.505	44.817	1.00	53.13	8
	ATOM	312	N	LEU		39	53.485	29.438	43.433		53.46	7
20	ATOM ATOM	313	CA	LEU		39	53.527	30.757	44.045		55.16	6
20	ATOM	314 315	CB CG	LEU		39 39	53.350 54.330	31.806	42.952		54.91	6
	ATOM	316		LEU		39	54.108	31.591 32.647	41.800 40.728		57.26 54.71	6 6
	ATOM	317		LEU		39	55.757	31.623	42.341		54.71	6
	ATOM	318	С	LEU		39	52.613	31.098	45.203		56.69	6
25	ATOM	319	0	LEU	Α	39	53.043	31.750	46.157		59.24	8
	ATOM	320	N	GLU		40	51.352	30.715	45.123	1.00	56.60	7
	ATOM	321	CA	GLU		40	50.451	31.019	46.216		58.75	6
	ATOM ATOM	322 323	CB CG	GLU GLU		40 40	49.617	32.251	45.920		59.61	6
30	ATOM	324	CD	GLU		40	50.426 49.547	33.520 34.752	45.821 45.683		65.69 69.26	6
	ATOM	325		GLU		40	48.747	34.732	44.715		72.53	6 8
	ATOM	326	OE2	GLU		40	49.655	35.659	46.543		69.31	8
	ATOM	327	С	GLU	Α	40	49.534	29.863	46.448		60.49	6
O.E.	ATOM	328	0	GLU		40	49.006	29.275	45.509	1.00	62.83	8
35	ATOM	329	N	VAL		41	49.348	29.525	47.710		60.13	7
	ATOM ATOM	330 331	CA CB	VAL		41	48.474	28.431	48.049		60.14	6
	ATOM	332		VAL VAL		41 41	49.292 48.376	27.230 26.185	48.576 49.146		59.98	6
	MOTA	333		VAL		41	50.118	26.632	47.444		59.73 59.26	6 6
40	ATOM	334	С	VAL		41	47.510	28.934	49.109		60.58	6
	MOTA	335	0	VAL	Α	41	47.864	29.793	49.934		61.24	8
	MOTA	336	N	ASN		42	46.283	28.428	49.059		59.54	7
	MOTA	337	CA	ASN		42	45.267	28.806	50.024		60.72	6
45	ATOM ATOM	338 339	CB CG	ASN ASN		42	44.346	29.895	49.463		59.36	6
	ATOM	340		ASN		42 42	43.473 42.811	30.530 29.835	50.533 51.303		59.07 60.43	6
	ATOM	341		ASN		42	43.462	31.856	50.582		57.17	8 7
	MOTA	342	С	ASN		42	44.474	27.535	50.286		62.57	6
	MOTA	343	0	ASN		42	43.654	27.107	49.460		62.42	8
50	ATOM	344	N	GLU		43	44.731	26.921	51.435	1.00	63.02	7
	ATOM	345	CA	GLU		43	44.045	25.695	51.792		62.62	6
	ATOM ATOM	346 347	CB CG	GLU GLU		43 43	44.772	25.004	52.942		65.20	6
	ATOM	348	CD	GLU		43	44.206 45.088	23.642 22.827	53.253 54.174		67.62 69.40	6 6.
55	ATOM	349		GLU		43	44.628	21.739	54.581		71.48	8
	ATOM	350	OE2	GLU		43	46.228	23.256	54.479		67.83	8
	ATOM	351	С	GLU	Α	43	42.595	25.959	52.169		61.53	6
	ATOM	352	0	GLU		43	41.755	25.058	52.086		59.68	. 8
60	MOTA MOTA	353 354	N	ILE		44	42.309	27.197	52.575		60.06	7
	ATOM	354 355	CA CB	ILE		44 44	40.957 40.923	27.580 28.953	52.951		60.59	6
		-00		تبست			40.743	40.333	53.632	1.00	84.00	6

	WO 01/58	951								PCT/EP01/01	457
							-78				
	ATOM	356	CG2	ILE	<b>A</b> (	14	39.469	29.343	53.943	1.00 61.06	6
	ATOM	357		ILE		14	41.749	28.921	54.918	1.00 61.51	6
	MOTA	358		ILE		14	41.119	28.117	56.022	1.00 61.37	6
_	MOTA	359	С	ILE	A . 4	14	40.069	27.660	51.718	1.00 61.06	6
5	MOTA	360	0	ILE		14	38.942	27.148	51.708	1.00 61.53	8
	ATOM	361	N	THR		15	40.581	28.302	50.674	1.00 60.25	7
	ATOM ATOM	362 363	CA CB	THR THR		15 15	39.826 40.086	28.464 29.844	49.426	1.00 58.34	6
	ATOM	364		THR		15	41.492	29.992	48.805 48.535	1.00 58.12 1.00 58.85	6 8
10	ATOM	365		THR		15	39.632	30.934	49.762	1.00 56.98	6
	ATOM	366	С	THR		15	40.139	27.407	48.374	1.00 56.43	6
	MOTA	367	0	THR	A 4	15	39.465	27.328	47.349	1.00 54.64	8
	MOTA	368	N	ASN		16	41.169	26.607	48.620	1.00 55.73	7
4.5	ATOM	369	CA	ASN			41.534	25.563	47.677	1.00 56.27	6
15	ATOM	370	CB	ASN		16	40.390	24.557	47.560	1.00 55.82	6
	ATOM ATOM	371 372	CG OD1	ASN ASN		16 16	40.612 39.671	23.327 22.621	48.412 48.746	1.00 56.92 1.00 55.85	6
	ATOM	372		ASN		16	41.866	23.058	48.754	1.00 55.85	8 7
	ATOM	374	C	ASN		16	41.869	26.127	46.299	1.00 56.62	6
20	MOTA	375	0	ASN		16	41.350	25.659	45.283	1.00 58.80	8
	ATOM	376	N	GLU	A 4	17	42.744	27.130	46.275	1.00 54.91	7
	ATOM	377	CA	GLU		17	43.156	27.766	45.044	1.00 52.39	6
	ATOM	378	CB	GLU		17	42.606	29.183	44.999	1.00 50.63	6
25	ATOM ATOM	379 380	CG CD	GLU		17	41.107	29.247	44.938	1.00 48.77	6
20	ATOM	381		GLU		17 17	40.601 41.370	30.675 31.577	44.951 44.568	1.00 53.28 1.00 51.68	6 8
	MOTA	382		GLU		17	39.429	30.902	45.333	1.00 51.08	8
	ATOM	383	C	GLU		17	44.671	27.776	44.979	1.00 52.87	6
	ATOM	384	0	GLU		17	45.347	28.009	45.981	1.00 53.20	8
30	ATOM	385	N	VAL		18	45.208	27.513	43.797	1.00 53.53	7
	MOTA	386	CA	VAL		18	46.656	27.481	43.619	1.00 53.36	. 6
	MOTA	387	CB	VAL		18	47.147	26.043	43.318	1.00 53.31	6
	ATOM ATOM	388 389		VAL VAL		18 18	48.646 46.781	26.029 25.130	43.122 44.456	1.00 55.73 1.00 52.72	6 6
35	ATOM	390	C	VAL		18	47.108	28.390	42.484	1.00 52.72	6
	ATOM	391	Ō	VAL		18	46.441	28.504	41.454	1.00 54.54	8
	ATOM	392	N	ASP	A 4	19	48.242	29.046	42.691	1.00 52.21	7
	ATOM	393	CA	ASP		19	48.818	29.928	41.692	1.00 51.57	6
40	ATOM	394	CB	ASP		19	49.084	31.291	42.304	1.00 52.64	6
40	MOTA	395	CG CD1	ASP		19	49.264	32.352	41.268	1.00 53.86	6
	MOTA MOTA	396 397 -		ASP ASP		19 19	49.900 48.779	32.051 33.482	40.246 41.474	1.00 54.56 1.00 57.00	8
	ATOM	398	C	ASP		19	50.121	29.241	41.313	1.00 50.45	8 6
	ATOM	399	Ō	ASP		19	51.074	29.254.	42.075	1.00 52.15	8
45	ATOM	400	N	VAL		60	50.155	28.636	40.135	1.00 49.83	7
	MOTA	401	CA	VAL		0	51.329	27.893	39.711	1.00 49.77	6
	ATOM	402	CB	VAL		0	50.992	26.372	39.723	1.00 51.61	6
	MOTA	403		VAL		0	50.095	26.015	38.531	1.00 51.90	6
50	MOTA MOTA	404 405	CGZ	VAL VAL		50 50	52.265 51.890	25.539 28.290	39.721 38.335	1.00 53.03 1.00 49.01	6
00	MOTA	406	o	VAL		50	51.193	28.230	37.508	1.00 49.01	6 8
	ATOM	407	N	VAL		1	53.163	27.974	38.117	1.00 46.39	7
	ATOM	408	CA	VAL		1	53.863	28.245	36.861	1.00 45.41	6
	ATOM	409	CB	VAL		1	55.111	29.134	37.083	1.00 43.93	6
55	MOTA	410		VAL		1	55.943	29.182	35.807	1.00 42.09	6
	ATOM ATOM	411		VAL		51 51	54.696	30.536	37.497	1.00 41.05	6
	ATOM	412 413	C O	VAL VAL		51 51	54.336 54.879	26.899 26.063	36.291 37.016	1.00 46.83 1.00 47.95	6 8
	ATOM	414	N	PHE		52	54.147	26.684	34.996	1.00 47.93	7
60	ATOM	415	CA	PHE		2	54.560	25.423	34.402	1.00 44.58	6
	ATOM .	416	CB	PHE		2	53.485	24.373	34.662	1.00 44.09	6

WO 01/58951			PCT/EP01/01457

						-79					
	ATOM	417	CG	PHE A	52	52.155	24.718	34.068	1.00 43	3.27	6
	ATOM	418		PHE A	52	51.857	24.393	32.758	1.00 42	2.79	6
	ATOM	419	CD2	PHE A	52	51.211	25.411	34.805	1.00 45		6
	MOTA	420	CE1	PHE A	52	50.643	24.755	32.194	1.00 43	L.86	6
5	MOTA	421	CE2	PHE A	52	49.991	25.776	34.240	1.00 49		6
	MOTA	422	CZ	PHE A	52	49.712	25.445	32.933	1.00 43		6
	MOTA	423	C	PHE A	52	54.789	25.547	32.906	1.00 49		6
	ATOM	424	0	PHE A	52	54.403	26.536	32.288	1.00 4		8
4.0	MOTA	425	N	TRP A	53	55.431	24.541	32.328	1.00 4		7
10	MOTA	426	CA	TRP A	53	55.662	24.527	30.898	1.00 40		6
	ATOM	427	CB	TRP A	53	57.043	24.000	30.573	1.00 48		6
	MOTA	428	CG	TRP A	53	58.137	24.899	30.983	1.00 50		6 6
•	ATOM	429	CD2	TRP A	53 53	59.531 60.213	24.604 25.755	30.942 31.386	1.00 5		6
15	ATOM ATOM	430 431	CE2	TRP A	53	60.274	23.473	30.570	1.00 5		6
13	ATOM	432		TRP A	53		26.175	31.436	1.00 5		6
	ATOM	433	NE1		53	59.267	26.700	31.682	1.00 5		7
	ATOM	434		TRP A	53	61.605	25.817	31.470	1.00 5		6
	ATOM	435		TRP A	53	61.660	23.527	30.649	1.00 5		6
20	ATOM	436	CH2	TRP A	53	62.314	24.697	31.099	1.00 5		6
	ATOM	437	C	TRP A	53	54.644	23.599	30.285	1.00 4		6
	ATOM	438	0	TRP A	53	54.645	22.410	30.564	1.00 4	9.29	8
	ATOM .		N	GLN A	54	53.765	24.139	29.457	1.00 4	7.91	7
	MOTA	440	CA	GLN A	54	52.765	23.312	28.825	1.00 4	8.38	6
25	MOTA	441	CB	GLN A	54	51.517	24.132	28.529	1.00 4		6
	MOTA	442	CG	GLN A	54	50.322	23.309	28.095	1.00 5		6
	ATOM	443	CD	GLN A	54	49.001	24.016	28.375	1.00 5		6
	MOTA	444		GLN A	54	48.697	24.360	29.515	1.00 5		8
00	ATOM	445		GLN A	54	48.209	24.231	27.335	1.00 5		. 7
30	ATOM	446	C	GLN A	54	53.378	22.755	27.555	1.00 4		6
	ATOM	447	0	GLN A	54	53.095	23.203	26.453	1.00 5		8 7
	ATOM	448	N	GLN A	55	54.251 54.937	21.779 21.122	27.738 26.641	1.00 5 1.00 5		6
	ATOM ATOM	449 450	CA CB	GLN A	55 55	55.995	20.200	27.234	1.00 5		6
35	ATOM	451	CG	GLN A	55	56.699	19.288	26.263	1.00 6		6
00	ATOM	452	CD	GLN A	55	57.909	18.634	26.907	1.00 7		6
	ATOM	453		GLN A	55	57.890	18.307	28.107	1.00 7		8
	ATOM	454	NE2		55	58.969	18.442	26.123	1.00 7		7
	ATOM	455	C	GLN A	55	53.939	20.353	25.774	1.00 5	1.30	6
40	ATOM	456	0	GLN A	55	53.451	19.293	26.151	1.00 5	0.67	8
	ATOM	457	N	THR A	56	53.648	20.907	24.604	1.00 4	9.14	7
	MOTA	458	CA	THR A	56	52.690	20.325	23.684	1.00 4		6
	ATOM	459	CB	THR A	56	51.597	21.347	23.342	1.00 4	5.67	6
	ATOM	460	OG1	THR A	56	51.138	21.969	24.541	1.00 4		8
45	MOTA	461	CG2	THR A	56	50.426	20.673	22.666	1.00 4		6
	ATOM	462	C	THR A	56	53.344	19.878	22.389	1.00 4		6
	MOTA	463	0	THR A	56	54.286	20.503	21.917	1.00 4		8
	ATOM	464	N	THR A	57	52.836	18.796	21.812	1.00 4		7
50	ATOM	465	CA	THR A	57	53.384	18.286	20.569	1.00 4 1.00 4		6 6
30	MOTA	466	CB	THR A	57 57	54.511	17.270 17.914	20.823 21.499	1.00 4		8
	ATOM ATOM	467 468		THR A	57 57	55.593 55.036	16.733	19.512	1.00 4		6
	ATOM	469	CGZ	THR A	57	52.316	17.627	19.721	1.00 4		6
	ATOM	470	ŏ	THR A	57	51.377	17.039	20.239	1.00 4		8
55	ATOM	471	N	TRP A	58	52.452	17.753	18.410	1.00 4		7
- <b>-</b>	ATOM	472	CA	TRP A	58	51.502	17.153	17.489	1.00 4		6
	MOTA	473	CB	TRP A	58	50.139	· 17.883	17.529	1.00 4	2.24	6
	MOTA	474	CG	TRP A	58	50.130	19.267	16.967	1.00 4		· 6
	ATOM	475		TRP A	58	50.427	20.473	17.668	1.00 3		6
60	MOTA	476		TRP A	58	50.354	21.521	16.735	1.00 4		6
	ATOM	477	CE3	TRP A	58	50.755	20.770	18.995	1.00 3	6.98	6

	WO 01/589	51								PCT/EP01/014	57
							-80				
	ATOM	478	CD1	TRP	Α	58	49.887	19.624	15.677	1.00 39.98	6
	ATOM	479	NE1			58	50.019		15.527	1.00 41.55	7
	MOTA	480		TRP		58	50.599		17.084	1.00 40.32	6
_	MOTA	481	CZ3	TRP	Α	58	50.997	22.081	19.341	1.00 37.03	6
5	ATOM	482	CH2	TRP	Α	58	50.919		18.389	1.00 38.53	6
	ATOM	483	С	TRP		58	52.112		16.098	1.00 47.09	· 6
	ATOM	484	0	TRP		58	53.226		15.915	1.00 47.06	8
	ATOM	485	N	SER		59	51.390		15,115	1.00 48.64	7
10	MOTA	486	CA	SER		59	51.933	16.631	13.782	1.00 50.92	6
10	ATOM ATOM	487 488	CB OG	SER		59	52.245	15.187	13.435	1.00 53.25	б
	ATOM	489	C	SER SER		59 59	53.191	15.109	12.389	1.00 62.80	8
	ATOM	490	0	SER		59	51.020 49.828		12.735	1.00 52.80	6
	ATOM	491	Ŋ	ASP		60	51.602	16.942 18.065	12.696 11.881	1.00 53.05	8
15	MOTA	492	CA	ASP		60	50.881	18.721	10.792	1.00 55.45 1.00 57.44	7 6
	ATOM	493	СВ	ASP		60	50.741	20.221	11.071	1.00 57.33	6
	MOTA	494	CG	ASP		60	49.856	20.936	10.058	1.00 57.43	6
	ATOM	495	OD1	ASP	Α	60	49.776	20.486	8.896	1.00 57.47	8
	MOTA	496		ASP		60	49.256	21.967	10.424	1.00 56.76	8
20	ATOM	497	C	ASP	Α	60	51.726	18.510	9.541	1.00 59.20	6
	MOTA	498	0	ASP	Α	60	52.679	19.245	9.304	1.00 58.82	8
	MOTA	499	N	ARG		61	51.372	17.503	8.748	1.00 61.30	7
	ATOM	500	CA	ARG		61	52.115	17.181	7.533	1.00 63.09	6
25	ATOM	501	CB	ARG		61	51.643	15.845	6.958	1.00 67.23	6
25	ATOM	502	CG	ARG		61	52.191	14.594	7.653	1.00 72.92	6
	ATOM	503	CD	ARG		61	51.883	13.355	6.786	1.00 81.01	6
	ATOM ATOM	504 505	NE CZ	ARG ARG		61 61	52.441	12.091	7.291	1.00 85.79	7
	ATOM	506		ARG		61	52.320 51.665	10.917	6.660	1.00 87.50	6
30	ATOM	507		ARG		61	52.852	10.843 9.815	5.501 7.179	1.00 88.31 1.00 87.74	7
	ATOM	508	C	ARG		61	52.073	18.238	6.430	1.00 61.74	7 6
	ATOM	509	Ō	ARG		61	52.927	18.225	5.550	1.00 61.39	8
	ATOM	510	N	THR		62	51.095	19.141	6.461	1.00 60.78	7
	MOTA	511	CA	THR	Α	62	51.017	20.175	5.434	1.00 59.76	6
35	ATOM	512	СВ	THR	Α	62	49.666	20.952	5.483	1.00 60.01	6
	MOTA	513		THR		62	49.582	21.720	6.689	1.00 62.71	8
	ATOM	514		THR	A	62	48.500	20.000	5.442	1.00 59.86	6
	ATOM	515	C	THR		62	52.172	21.171	5.616	1.00 58.73	6
40	ATOM ATOM	516 517	0	THR		62	52.400	22.044	4.774	1.00 59.33	8
70	ATOM	517 518	N	LEU		63	52.898	21.031	6.720	1.00 56.50	7
	ATOM	519	CA CB	LEU		63 63	54.029 54.088	21.903	7.020	1.00 55.97	6
	MOTA	520	CG	LEU		63	52.866	22.205 22.837	8.521	1.00 53.19	6
	ATOM	521		LEU		63	53.074	22.837	9.174 10.672	1.00 52.76 1.00 51.73	6
45	ATOM	522		LEU		63	52.629	24.217	8.589	1.00 51.73	6 6
	MOTA	523	С	LEU		63	55.351	21.264	6.603	1.00 55.80	6
	MOTA	524	0	LEU		63	56.366	21.947	6.509	1.00 54.36	8
	MOTA	525	N	ALA	Α	64	55.332	19.952	6.368	1.00 56.30	7
<b>-</b> 0	MOTA	526	CA	ALA		64	56.532	19.207	5.987	1.00 56.99	6
50	ATOM	527	CB	ALA		64	56.194	17.744	5.810	1.00 54.20	6
	MOTA	528	C	ALA		64	57.176	19.745	4.715	1.00 59.20	б
	MOTA	529	0	ALA		64	56.487	20.224	3.816	1.00 60.08	8
	MOTA	530 531	N	TRP		65	58.502	19.646	4.651	1.00 60.65	7
55	ATOM ATOM	531 532	CA CB	TRP TRP		65 65	59.295 59.623	20.104	3.506	1.00 62.47	6
	ATOM	533	CG	TRP		65	60.773	21.588 21.870	3.667	1.00 59.37	6
	MOTA	534		TRP		65	60.685	22.167	4.613 6.020	1.00 56.94 1.00 56.89	6
	ATOM	535		TRP		65	62.001	22.424	6.475	1.00 55.08	6 6
	ATOM	536		TRP		65	59.622	22.245	6.938	1.00 54.01	6
60	ATOM	537	CD1	TRP	Α	65	62.097	21.947	4.292	1.00 55.45	6
	MOTA	538	NE1	TRP	A	65	62.838	22.282	5.400	1.00 53.98	7

	WO 01/58	951								PCT/EP01/01	457
							-81				
	ATOM	539	CZ2	TRP .	A 6	5	62.286	22.757	7.808	1.00 52.03	6
	ATOM	540	CZ3	TRP :	A 6	5	59.910	22.577	8.266	1.00 53.82	6
	ATOM	541	CH2	TRP .	A 6	5	61.232	22.829	8.684	1.00 51.71	6
	MOTA	542	С	TRP .		5	60.603	19.297	3.445	1.00 65.72	6
5	ATOM	543	0	TRP .	A 6	5	61.091	18.825	4.479	1.00 66.89	8
	MOTA	544	N	ASN .	A 6	6	61.181	19.138	2.255	1.00 68.69	7
	ATOM	545	CA	ASN .	A 6	6	62.431	18.371	2.149	1.00 71.84	6
	ATOM	546	CB	ASN .		6	62.735	17.983	0.689	1.00 73.23	6
	MOTA	547	CG	ASN .		6	63.968	17.084	0.568	1.00 76.18	6
10	MOTA	548	OD1	ASN .		6	64.473	16.822	-0.541	1.00 76.68	8
	ATOM	549	ND2	ASN		6	64.463	16.606	1.715	1.00 76.39	7
	ATOM	550	С	ASN		6	63.581	19.199	2.723	1.00 71.96	6
	ATOM	551	0	ASN		6	63.902	20.279	2.217	1.00 72.02	8
4 -	MOTA	552	N	SER		57	64.197	18.690	3.784	1.00 72.09	7
15	MOTA	553	CA	SER		7	65.292	19.403	4.435	1.00 72.65	6
	ATOM	554	CB	SER		7	65.063	19.425	5.943	1.00 72.61	6
	MOTA	555	OG G	SER		7	64.969	18,105	6.449	1.00 70.09 1.00 73.27	8 6
	MOTA	556	C	SER		57 57	66.655 67.576	18.794 19.031	4.177 4.961	1.00 73.27	8
20	ATOM ATOM	557 558	N O	SER SER		8	66.799	18.026	3.097	1.00 72.43	7
20	ATOM	559	CA	SER		8	68.082	17.370	2.825	1.00 76.38	6
	ATOM	560	CB	SER		8	68.002	16.490	1.564	1.00 75.57	6
	ATOM	561	OG	SER		8	67.870	17.265	0.386	1.00 75.20	8
	ATOM	562	C	SER		8	69.222	18.380	2.707	1.00 77.15	6
25	ATOM	563	Ö	SER		8	70.288	18.201	3.300	1.00 77.04	8
	ATOM	564	N	HIS		59	68.992	19.451	1.962	1.00 78.21	7
	ATOM	565	CA	HIS		59	70.015	20.479	1.804	1.00 79.62	6
-	ATOM	566	CB	HIS		59	70.445	20.578	0.341	1.00 84.04	6
	MOTA	567	CG	HIS	A 6	59	71.007	19.302	-0.196	1.00 88.01	6
30	MOTA	568	CD2	HIS	A 6	59	72.208	19.022	-0.759	1.00 89.20	6
	MOTA	569	ND1	HIS	A 6	59	70.332	18.100	-0.110	1.00 89.31	7
	MOTA	570	CE1	HIS		59	71.096	17.133	-0.589	1.00 90.18	6
	ATOM	571	NE2	HIS		59	72.240	17.666	-0.988	1.00 90.99	7
	MOTA	572	С	HIS		59	69.441	21.799	2.279	1.00 77.78	6
35	MOTA	573	0	HIS		59	69.473	22.803	1.561	1.00 77.92	8
	MOTA	574	N	SER		70	68.896	21.766	3.496	1.00 75.27	7
,	ATOM	575	CA	SER		70	68.300	22.931	4.141	1.00 72.21	6
	ATOM	576	CB	SER		70	67.013	23.316	3.421	1.00 72.74 1.00 74.05	6 8
40	MOTA	577	OG	SER		70	66.368	22.158	2.919	1.00 74.05	6
40	ATOM	578 570	C	SER		70 70	68.031 68.138	22.563 21.384	5.595 5.962	1.00 70.38	8
	ATOM ATOM	579 580	N	SER PRO		70 71	67.710	23.563	6.450	1.00 70.38	7
	ATOM	581	CD	PRO		71	67.819	24.998	6.134	1.00 64.03	6
	ATOM	582	CA	PRO		71	67.422	23.385	7.883	1.00 64.80	6
45	ATOM	583	CB	PRO		71	67.106	24.805	8.334	1.00 63.49	6
	ATOM	584	CG	PRO		71	68.031	25.608	7.498	1.00 61.83	6
	ATOM	585	C	PRO		71	66.295	22.395	8.223	1.00 63.99	6
	ATOM	586	0	PRO		71	65.314	22.289	7.496	1.00 63.63	8
	ATOM	587	N	ASP		72	66.434	21.679	9.333	1.00 63.39	7
50	MOTA	588	CA	ASP		72	65.424	20.701	9.734	1.00 63.43	6
	MOTA	589	CB	ASP	A :	72	66.056	19.634	10.617	1.00 65.69	6
	MOTA	590	CG	ASP		72	67.229	18.974	9.959	1.00 70.53	6
	MOTA	591		ASP		72	66.985	18.216	8.988	1.00 73.68	8
	ATOM	592		ASP		72	68.389		10.390	1.00 71.00	8
55	MOTA	593	C	ASP		72	64.307	21.356	10.520	1.00 62.20	6
	MOTA	594	0	ASP		72	63.164	20.878	10.520	1.00 61.88	8
	ATOM	595	N	GLN		73	64.653	22.457	11.175	1.00 59.83	7
	MOTA	596	CA	GLN		73	63.738	23.186	12.041	1.00 59.45	6
60	MOTA	597	CB	GLN		73 73	64.083 63.720	22.901 21.569	13.489 14.035	1.00 60.33 1.00 63.59	6 6
00	MOTA MOTA	598 599	CG	GLN GLN		73	64.224	21.462	15.459	1.00 68.15	6
	ET OH	333	CD.	CTITA	**		04.224	22,402			•

								-82					
	MOTA	600	OE1	GLN .	A	73		65.425	21.595	15.699	1.00	70.61	8
	ATOM	601		GLN .		73		63.316	21.249	16.416	1.00	69.73	7
	ATOM .	602	С	GLN .	A	73		63.779	24.703	11.886	1.00		6
	ATOM	603	0	GLN .	Α	73		64.798	25.280	11.490	1.00	58.19	8
5	ATOM	604	N	VAL .	A	74		62.670	25.336	12.243	1.00 9		7
	MOTA	605	CA	VAL	A	74		62.557	26.782	12.211	1.00		6
	MOTA	606	CB	VAL .	Α	74		62.036	27.279	10.859	1.00		6
	MOTA	607	CG1	VAL .	A	74		63.066	27.034	9.794	1.00		6
	MOTA	608	CG2	VAL	A	74		60.738	26.584	10.515	1.00		6
10	MOTA	609	C	VAL		74		61.580	27.201	13.310	1.00		6
	MOTA	610	0	VAL		74		60.756	26.401	13.754	1.00		8
	MOTA	611	N	SER		75		61.691	28.442	13.769	1.00		7
	MOTA	612	CA	SER		75		60.792	28.954	14.787	1.00		6
4.5	MOTA	613	CB	SER		75		61.525	29.902	15.728	1.00		6 8
15	ATOM	614	OG	SER		75		62.241	29.188	16.710	1.00		6
	MOTA	615	C	SER		75 75		59.668 59.894	29.688 30.657	14.084 13.358	1.00		8
	MOTA	616	0	SER VAL		76		58.451	29.214	14.307	1.00		7
	MOTA	617 618	N CA	VAL		76		57.272	29.792	13.687	1.00		6
20	ATOM ATOM	619	CB	VAL		76		56.482	28.711	12.936	1.00		6
20	ATOM	620		VAL		76		55.247	29.315	12.298		44.97	6
	ATOM	621	CG2			76		57.359	28.058	11.894		43.12	6
	ATOM	622	C	VAL		76		56.335	30.436	14.704		44.16	6
	ATOM	623	ō	VAL		76		56.093	29.882	15.773	1.00	45.89	8
25	ATOM	624	N	PRO		77		55.798	31.624	14.388	1.00	43.19	7
	ATOM	625	CD	PRO	Α	77		56.162	32.556	13.311	1.00	41.24	6
	ATOM	626	CA	PRO	Α	77		54.884	32.266	15.334	1.00	41.49	6
	ATOM	627	CB	PRO	Α	77		54.619	33.615	14.691	1.00	41.13	6
	ATOM	628	CG	PRO	Α	77		55.886	33.884	13.950		41.89	6
30	MOTA	629	C	PRO	Α	77		53.617	31.439	15.453		40.82	6
	MOTA	630	0	PRO		77		53.112	30.919	14.471		39.55	8
	MOTA	631	N	ILE		78		53.116	31.318	16.671		42.42	7
	MOTA	632	CA	ILE		78		51.908	30.556	16.959		42.14	6
0.5	MOTA	633	CB	ILE		78		51.526	30.751	18.441		42.09	6
35	ATOM	634	CG2	ILE		78		50.105	30.357	18.712		43.53 43.22	6 6
	MOTA	635	_	ILE		78 78	. ·	52.464 52.585	29.921 28.513	19.285 18.784		43.22	6
	MOTA MOTA	636	CDI	ILE		78		50.749	30.942	16.057		43.58	6
	ATOM	637 638	0	ILE		78		49.985	30.096	15.624		45.64	8
40	ATOM	639	Ŋ	SER		79	*	50.642	32.229	15.768		43.79	7
40	ATOM	640	CA	SER		79		49.588	32.767	14.918		44.38	6
	MOTA	641	СВ	SER		79		49.666	34.292	14.934		44.81	6
	ATOM	642	OG .	SER		79		50.972	34.732	14.584	1.00	45.88	8
	MOTA	643	C	SER		79		49.590	32.295	13.465	1.00	43.50	6
45	ATOM	644	0	SER	Α	79		48.607	32.498	12.758	1.00	42.80	8
	MOTA	645	N	SER	Α	80		50.685	31.683	13.016.		42.62	7
	MOTA	646	CA	SER	Α	80		50.774	31.216	11.639		42.84	6
	MOTA	647	CB	SER	A	80		52.137	31.555	11.043		44.68	6
	MOTA	648	OG	SER		80		52.308	32.956	10.932		51.59	8
50	MOTA	649	С	SER		80		50.534	29.726	11.502		44.69	б
	MOTA	650	0	SER		80		50.596	29.184	10.402		43.97	8
	ATOM	651	N	LEU		81		50.248	29.068	12.620		45.13 41.19	7
	MOTA	652	CA	LEU		81		50.003	27.631	12.631		39.92	6 6
55	MOTA	653		LEU		81		51.061	26.926 27.167	13.467 13.185		41.52	6
55	ATOM ATOM	654 655	CG CD1	LEU		81 81		52.534 53.356	26.677	14.355		39.70	.6
	ATOM	656		LEU		81		52.922	26.464	11.918		42.52	6
	ATOM	657	C	LEU		81		48.672	27.340	13.272		39.47	6
	MOTA	658	Ö	LEU		81		48.089	28.197	13.921		40.21	8
60	ATOM	659	N	TRP		82		48.191	26.122	13.081		38.46	7
	MOTA	660	CA	TRP		82		46.965	25.694	13.720	1.00	37.32	6

	WO 01/589	51							PCT/EP01/014	157
						-83				
	ATOM	661	СВ	TRP A	. 82	46.346	24.494	13.006	1.00 36.83	6
	ATOM	662	CG	TRP A		45.274	23.818	13.829	1.00 40.60	6 6
	ATOM	663		TRP A		45.459	22.741	14.757	1.00 39.63	6
	ATOM	664		TRP A		44.213	22.499	15.369	1.00 38.33	6
5	ATOM	665		TRP A		46.560	21.961	15.132	1.00 40.54	6
	MOTA	666		TRP A		43.948	24.170	13.914	1.00 39.43	. 6
	MOTA	667	NE1	TRP A	. 82	43.311	23.383	14.839	1.00 39.00	7
	ATOM	668		TRP A		44.040	21.511	16.332	1.00 38.94	6
40	MOTA	669		TRP A		46.388	20.982	16.088	1.00 39.99	6
10	MOTA	670		TRP A		45.135	20.764	16.678	1.00 39.88	6
	ATOM	671	C	TRP A		47.485	25.241	15.064	1.00 36.99	6
	ATOM	672	0	TRP A		48.559	24.661	15.142	1.00 38.93	8
	ATOM ATOM	673 674	N	VALA		46.744	25.503	16.123	1.00 37.43	7
15	ATOM	675	CA CB	VAL A		47.179 47.729	25.086 26.300	17.437 18.209	1.00 37.48	6
	MOTA	676		VALA		47.729	25.984	19.655	1.00 37.40 1.00 43.51	6 6
	ATOM	677		VAL A		49.054	26.688	17.644	1.00 43.31	6
	ATOM	678	C	VAL A		46.011	24.437	18.175	1.00 37.34	6
	MOTA	679	0	VAL A		44.858	24.823	17.997	1.00 42.50	8
20	MOTA	680	N	PRO A		46.290	23.408	18.982	1.00 39.54	7
	ATOM	681	CD	PRO A	84	47.594	22.745	19.134	1.00 41.22	6
	MOTA	682	CA	PRO A		45.263	22.701	19.752	1.00 38.54	6
	ATOM	683	CB	PRO A		46.079	21.690	20.558	1.00 39.94	6
25	ATOM	684	CG	PRO A		47.202	21.381	19.663	1.00 41.42	6
25	ATOM	685	С	PRO A		44.509	23.663	20.658	1.00 36.09	6
	ATOM ATOM	686 687	N O	PRO A		45.121	24.469	21.342	1.00 35.57	8
	ATOM	688	CA.	ASP A		43.186 42.397	23.576 24.458	20.668 21.505	1.00 32.88 1.00 34.36	7 6
	ATOM	689	CB	ASP A		41.014	24.458	20.898	1.00 34.36	6
30	ATOM	690	CG	ASP A			23.381	20.696	1.00 33.14	6
•	MOTA	691		ASP A		40.897	22.388	20.290	1.00 40.24	8
	MOTA	692	OD2	ASP A	. 85	39.050	23.367	20.927	1.00 37.65	8
	MOTA	693	С	ASP A		42.277	23.906	22.910	1.00 35.33	6
0.5	MOTA	694	0	ASP A		41.180	23.726	23.420	1.00 38.82	8
35	ATOM	695	N	LEU A		43.418	23.644	23.528	1.00 32.24	7
	MOTA MOTA	696 697	CA	LEU A		43.459	23.106	24.869	1.00 35.18	6
	ATOM	698	CB CG	LEU A		44.878 45.435	22.670	25.208	1.00 34.63	6
	ATOM	699		LEU A		46.842	21.585 21.241	24.311 24.749	1.00 35.36 1.00 34.84	6 6
40	ATOM	700		LEU A		44.530	20.376	24.749	1.00 34.64	6
	ATOM	701	C	LEU A		42.973	24.086	25.925	1.00 36.01	6
	MOTA	702	0	LEU A		43.141	25.283	25.800	1.00 37.75	8
•	MOTA	703	N	ALA A		42.378	23.556	26.979	1.00 38.03	7
4-	ATOM	704	CA	ALA A		41.870	24.369	28.060	1.00 38.29	6
45	MOTA	705	CB	ALA A		40.428	24.674	27.811	1.00 36.17	6
	MOTA	706	C	ALA A		42.022	23.605	29.371	1.00 41.08	6
	MOTA MOTA	707	0	ALA A		41.798	22.399	29.407	1.00 43.90	8
	ATOM	708 709	N CA	ALA A		42.431 42.558	24.290	30.436 31.726	1.00 39.68	7
50	ATOM	710	CB	ALA A		43.586	23.639 24.337	32.571	1.00 38.37 1.00 34.88	6 6
	ATOM	711	C	ALA A		41.180	23.729	32.376	1.00 40.65	6
	MOTA	712	Ō	ALA A		40.778	24.780	32.847	1.00 40.29	8
	ATOM	713	N	TYR A		40.460	22.613	32.371	1.00 42.49	7
	MOTA	714	CA	TYR A		39.116	22.502	32.934	1.00 44.24	6
55	ATOM	715	CB	TYR A		38.727	21.023	33.052	1.00 46.70	6
	MOTA	716	CG	TYR A	89	38.641	20.286	31.725	1.00 51.62	6
	ATOM	717		TYR A		38.462	18.902	31.684	1.00 54.35	6
	ATOM ATOM	718 719 /		TYR A	89 89	38.353 38.711	18.222 20.968	30.466	1.00 56.33	6
60	MOTA	720		TYR A		38.604	20.368	30.511 29.302	1.00 51.86 1.00 53.71	6 6
	MOTA	721	CZ	TYR A	89	38.424	18.927	29.286	1.00 55.54	6
									and the second s	

							-84				
	ATOM	722	OH	TYR .	A 8	19	38.296	18.257	28,093	1.00 59.35	8
	ATOM	723	C	TYR .		9	38.888	23.185	34.280	1.00 43.81	6
	ATOM	724	ō	TYR		39	37.808	23.735	34.518	1.00 41.70	8
	MOTA	725	N	ASN .	A 9	0	39.880	23.149	35.167	1.00 43.90	7
5	MOTA	726	CA	ASN .	A 9	0	39.709	23.781	36.473	1.00 43.12	6
	MOTA	727	CB	ASN .	A 9	0	39.976	22.770	37.598	1.00 40.92	6
	MOTA	728	CG	ASN	A 9	0	41.340	22.156	37.517	1.00 42.04	6
	ATOM	729	OD1	ASN .	A 9	0	41.770	21.721	36.456	1.00 43.62	8
	ATOM	730	ND2	ASN		90	42.033	22.102	38.646	1.00 43.25	7
10	MOTA	731	C	ASN		0	40.550	25.042	36.655	1.00 44.35	6
	ATOM	732	0	ASN		0	40.881	25.434	37.769	1.00 46.42	8
	MOTA	733	N	ALA		1	40.902	25.673	35.543	1.00 45.44	7
	ATOM	734	CA	ALA		)1	41.660	26.912	35.591	1.00 45.36	6
15	ATOM	735	CB	ALA		91	42.130	27.308	34.206	1.00 44.43	6
15	ATOM	736	С	ALA		)1 )1	40.680 39.522	27.940 28.000	36.136 35.729	1.00 45.00 1.00 43.71	6 8
	ATOM ATOM	737 738	N O	ALA ILE		92	41.164	28.750	37.064	1.00 45.71	7
	ATOM	739	CA	ILE		92	40.359	29.753	37.734	1.00 46.18	6
	ATOM	740	CB	ILE		92	40.674	29.673	39.232	1.00 47.56	6
20	ATOM	741	CG2			2	41.595	30.797	39.634	1.00 50.92	6
	ATOM	742	CG1	ILE		92	39.409	29.713	40.055	1 00 50.52	6
	ATOM	743		ILE		92	39.711	29.795	41.547	1.00 51.82	6
	ATOM	744	C	ILE		2 .	40.659	31.157	37.177	1.00 45.80	6
	ATOM	745	0	ILE		92	39.996	32.134	37.518	1.00 45.79	8
25	ATOM	746	N	SER		93	41.666	31,237	36.317	1.00 44.40	7
	ATOM	747	CA	SER	A 9	93	42.076	32.483	35.687	1.00 41.89	6
	MOTA	748	CB	SER	A 9	93	43.248	33.080	36.445	1.00 40.83	6
	ATOM	749	OG	SER		93	44.400	32.275	36.274	1.00 37.97	8
	MOTA	750	С	SER		93	42.541		34.295	1.00 42.18	6
30	MOTA	751	0	SER		93	42.762	30.942	34.023	1.00 41.06	8
	MOTA	752	N	LYS		94	42.693	33.081	33.401	1.00 43.27	7
	ATOM	753	CA	LYS		94	43.178	32.712	32.077	1.00 45.47	6
	ATOM	754	CB	LYS		94	42.703	33.680	30.988	1.00 44.26 1.00 44.49	6 6
35	ATOM ATOM	755 756	CG CD	LYS LYS		94 94	42.747 41.907	35.142 35.918	31.314 30.309	1.00 44.49	6
55	ATOM	757	CE	LYS		94 94	42.209		28.885	1.00 47.75	6
	ATOM	758	NZ	LYS		94	41.443		27.873	1.00 49.19	7
	ATOM	759	C	LYS		94	44.688	32.592	32.089	1.00 43.67	6
	ATOM	760	ŏ	LYS		94	45.359		32.980	1.00 44.46	8
40	MOTA	761	N	PRO		95	45.243		31.105	1.00 43.23	7
	ATOM	762	CD	PRO		95	44.559		30.004	1.00 41.03	6
	MOTA	763	CA	PRO	A S	95	46.692	31.695	31.024	1.00 42.80	6
	MOTA	764	CB	PRO	A :	95	46.858	30.719	29.862	1.00 43.77	6
	MOTA	765	CG	PRO	A :	95	45.515		29.725	1.00 43.00	6
45	ATOM	766	С	PRO		95	47.480		30.783	1.00 41.84	6
	MOTA	767	0	PRO		95	47.178		29.861	1.00 41.82	8
	MOTA	768	N	GLU		96.	48.483		31.627	1.00 40.74	7
	ATOM	769	CA	GLU		96	49.350		31.472	1.00 39.25	6
50	ATOM	770	CB	GLU		96	49.704		32.817	1.00 41.50	6
50	ATOM	771	CG	GLU		96	50.548		32.682	1.00 46.46 1.00 51.10	6
	MOTA	772	CD OF1	GLU		96 96	50.864 50.172		34.014 35.002	1.00 51.10	6 8
	MOTA MOTA	773 774		GLU		96	51.784		34.079	1.00 51.01	8
	MOTA	775	C	GLU		96	50.583		30.851	1.00 38.30	6
55	ATOM	776	0	GLU		96	51.424		31.548	1.00 37.33	8
	ATOM	777	N	VAL		97	50.662		29.528	1.00 36.80	7
	ATOM	778	CA	VAL		97	51.813		28.821	1.00 37.13	6
	ATOM	779	CB	VAL		97	51.514		27.313	1.00 35.99	6
_	MOTA	780	CG1	VAL		97	52.704	32.480	26.600	1.00 34.96	6
60	MOTA	781	CG2	VAL		97	50.287		27.122	1.00 30.36	6
	MOTA	782	С	VAL	A :	97	53.002	34.160	29.061	1.00 37.37	6

	WO 01/58	951					·			
						-85				
	ATOM	783	0	VAL A	97	52.998	35.329	28.670	1.00 35.14	8
	MOTA	784	N	LEU A	98	54.022	33.619	29.715	1.00 37.54	7
	MOTA	785	CA	LEU A	98	55.203	34.389	30.070	1.00 39.37	6
_	MOTA	786	CB	LEU A	98	55.773	33.851	31.374	1.00 38.96	6
5	ATOM	787	CG	LEU A	98	54.848	33.662 32.772	32.568 33.576	1.00 39.17 1.00 37.89	· 6
	MOTA	788		LEU A	98 98	55.522 54.501	34.997	33.376	1.00 37.05	6
	ATOM ATOM	789 790	CDZ	LEU A	98	56.317	34.387	29.033	1.00 41.78	6
	ATOM	791	ō	LEU A	98	57.310	35.114	29.177	1.00 42.77	8
10	ATOM	792	N	THR A	99	56.162	33.579	27.992	1.00 39.65	7
	MOTA	793	CA	THR A	99	57.199	33.471	26.981	1.00 37.85	6
	MOTA	794	CB	THR A	99	57.793	32.063	27.004	1.00 39.36	6 8
	MOTA	795		THR A	99	56.745 58.490	31.102 31.812	26.822 28.325	1.00 40.29 1.00 36.68	6
15	MOTA	796 797	CG2 C	THR A	99 99	56.762	33.784	25.559	1.00 37.27	6
15	MOTA MOTA	798	0	THR A		55.571	33.809	25.260	1.00 37.48	. 8
	MOTA	799	N	PRO A		57.733	34.050	24.666	1.00 35.48	7
	MOTA	800	CD	PRO A		59.169	34.217	24.938	1.00 34.88	6
	MOTA	801	CA	PRO A		57.450	34.356	23.268	1.00 34.86	6
20	ATOM	802	CB	PRO A		58.825 59.660	34.308 34.899	22.631 23.674	1.00 32.91 1.00 33.33	6 6
	MOTA	803 804	CG C	PRO A		56.535	33.287	22.735	1.00 34.32	6
	ATOM ATOM	805	0	PRO A		56.748	32.110	22.990	1.00 37.05	8
	MOTA	806	N	GLN A		55.508	33.684	22.005	1.00 35.52	7
25	ATOM	807	CA	GLN A		54.591	32.698	21.483	1.00 38.08	6
	MOTA	808	CB	GLN A		53.181	33.271	21.452	1.00 39.02	6
	MOTA	809	CG	GLN A		52.557	33.223	22.836	1.00 42.77 1.00 46.68	6 6
	MOTA	810	CD OF1	GLN A GLN A		51.356 50.383	34.102 33.943	22.965 22.239	1.00 51.63	8
30	ATOM ATOM	811 812	NE2			51.408	35.045	23.900	1.00 48.84	7
00	ATOM	813	C	GLN A		55.006	32.145	20.144	1.00 37.60	6
	ATOM	814	0	GLN A		54.331	32.329	19.136	1.00 36.16	8
	MOTA	815	N	LEU A		56.138	31.445	20.177	1.00 38.73	7
~~	ATOM	816	CA	LEU A		56.742	30.812	19.016	1.00 38.35	6 6
35	MOTA	817	CB	LEU A		58.180 58.411	31.289 32.792	18.833 18.709	1.00 37.99	6
	MOTA MOTA	818 819	CG CD1	LEU A		59.890	33.054	18.550	1.00 39.54	6
	ATOM	820		LEU A		57.650	33.343	17.538	1.00 35.40	6
	ATOM	821	C	LEU A		56.763	29.311	19.200	1.00 39.23	6
40	ATOM	822	0	LEU A	102	56.933	28.809	20.302	1.00 40.34	8
	ATOM	823	N	ALA A		56.574	28.595	18.104	1.00 40.83	7
	ATOM	824	CA	ALA A		56.603	27.142 26.569	18.125 17.497	1.00 41.49 1.00 41.49	6 6
	ATOM ATOM	825 826	CB C	ALA A		55.334 57.830	26.697	17.337	1.00 42.17	6
45	ATOM. ATOM	827	Ö	ALA A		58.472	27.484	16.645	1.00 43.45	8
	ATOM	828	N	ARG A		58.163	25.427	17.453	1.00 43.77	7
	MOTA	829	CA	ARG A	104	59.309	24,893	16.750	1.00 44.63	6
	MOTA	830	CB	ARG A		60.242	24.228	17.745	1.00 43.89	6
<b>-</b> 0	MOTA	831	CG	ARG A		61.621	23.992	17.214	1.00 45.78 1.00 43.65	6 6
50	MOTA	832	CD NE	ARG A		62.362 63.675	25.277 24.958	16.950 16.409	1.00 44.01	7
	MOTA MOTA	833 834	CZ		104	64.618	25.848	16.124	1.00 46.53	6
•	ATOM	835		L ARG		64.411	27.147	16.327	1.00 47.99	7
	ATOM	836		2 ARG	104	65.775	25.432	15.632	1.00 47.13	7
55	MOTA	837	С		A 104	58.770	23.878	15.754		6
	ATOM	838	0		A 104	58.042	22.961	16.124	1.00 49.12 1.00 47.69	8 7
	MOTA	839	N		A 105	59.097 58.601		14.482 13.469		6
	MOTA MOTA	840 841			A 105 A 105	57.791		12.382	,	6
60	ATOM	842		1 VAL		57.198		11.421		6
	ATOM	843		2 VAL		56.702		13.018		6

	WO 01/589	51							PCT/	EP01/014	157
						-86					
	ATOM	844	С	VAL A	1.05	59.731	22.355	12.799	1 00	49.71	6
	ATOM	845	ō	VAL A		60.688	22.946	12.283		48.12	8
	ATOM	846	N	VAL A		59.597	21.030	12.821		50.55	7
	ATOM	847	CA	VAL A		60.571	20.123	12.232		51.43	6
5	ATOM	848	СВ	VAL A		60.648	18.816	13.037		52.44	6
	ATOM	849		VAL A		61.828	17.987	12.571		50.24	. 6
	ATOM	850		VAL A		60.762	19.128	14.521		52.53	6
	ATOM	851	С	VAL A		60.142	19.809	10.805		52.38	6
	ATOM	852	0	VAL A		58.961	19.644	10.536		52.65	8
10	ATOM	853	N	SER A		61.101	19.718	9.895		52.34	7
	ATOM	854	CA	SER A	107	60.803	19.447	8.492		54.32	6
	ATOM	855	CB	SER A		62.111	19.185	7.735	1.00	55.62	6
	MOTA	856	OG	SER A	. 107	62.965	18.316	8.462	1.00	60.14	8
4-	MOTA	857	C	SER A	107	59.795	18.328	8.186	1.00	53.69	6
15	MOTA	858	0	SER A		59.191	18.304	7.111	1.00	51.90	8
	ATOM	859	N	ASP A		59.598	17.412	9.122	1.00	54.61	7
	ATOM	860	CA	ASP A		58.667	16.318	8.890	1.00	57.15	6
	ATOM	861	CB	ASP A		59.164	15.046	9.580		58.72	6
20	ATOM	862	CG	ASP A		59.114	15.134	11.097		61.68	6
20	MOTA	863		ASP A		59.391	16.221	11.642		64.28	8
	MOTA	864		ASP A		58.816	14.105	11.747		62.23	8
	ATOM	865	C	ASP A		57.235	16.615	9.320		58.57	6
	ATOM ATOM	866 867	0	ASP A		56.379	15.725	9.301		58.30	8
25	ATOM	868	N CA	GLY A		56.979	17.865	9.703		59.14	7
	ATOM	869	C	GLY A		55.649 55.397	18.271	10.116		58.25	6
	ATOM	870	0	GLY A		54.273	18.166 18.374	11.602		58.69	6
	ATOM	871	N	GLU A		56.423	17.821	12.054 12.369		59.98 58.71	8
	ATOM	872	CA	GLU A		56.255	17.713	13.813		58.33	7 6
30	MOTA	873	СВ	GLU A		57.380	16.871	14.425		61.59	6
	MOTA	874	CG	GLU A		57.062	16.242	15.797		66.10	6
	MOTA	875	CD	GLU A		55.913	15.218	15.728		70.89	6
	ATOM	876		GLU A		55.634	14.710	14.600		70.53	8
	MOTA	877		GLU A		55.303	14.916	16.800		70,77	8
35	MOTA	878	С	GLU A	110	56.293	19.136	14.369		56.59	6
	MOTA	879	0	GLU Ą	110	57.114	19.955	13.941		54.81	8
	MOTA	880	N	VAL A	111	55.392	19.425	15.307	1.00	54.27	7
		881	CA	VAL A	111	55.310	20.745	15.912	1.00	52.01	6
40	MOTA	882	CB	VAL A		53.949	21.412	15.616	1.00	50.79	6
40	MOTA	883		VAL A		53.902	22.795	16.242	1.00	47.90	6
	ATOM	884		VAL A			21.489				6
	ATOM	885	C	VAL A		55.465	20.666	17.418		51.33	6
	ATOM	886	0	VAL A		54.833	19.830	18.057		50.54	8
45	ATOM ATOM	887 888	N	LEU A		56.300	21.539	17.979		49.64	7
70	ATOM	889	CA CB	LEU A		56.501	21.569	19.418		50.36	6
	MOTA	890	CG	LEU A		57.911	21.107	19.791		54.86	6
	ATOM	891		LEU A		58.651	20.020	18.989		59.01	6
	ATOM	892		LEU A		57.699 59.248	18.865	18.631		60.90	6
50	ATOM	893	C	LEU A		56.297	20.632 22.980	17.727 19.946		57.28 49.94	6
	ATOM	894	ō	LEU A		57.004	23.893	19.553		49.38	6
	ATOM	895	N	TYR A		55.323	23.151	20.833		49.46	8 7
	ATOM	896	CA	TYR A		55.036	24.446	21.437		47.23	6
	MOTA	897	CB	TYR A		53.643		21.021		45.72	6
55	ATOM	898	CG	TYR A		53.222	26.279	21.621		46.02	6
	ATOM			TYR A		54.092	27.364	21.654		42.86	6
	MOTA	900	CE1	TYR A	113	53.691	28.588	22.179		43.03	6
	ATOM	901		TYR A		51.936	26.462	22.131		45.25	6
00	ATOM	902		TYR A		51.533	27.682	22.653		41.00	6
60	MOTA	903	CZ	TYR A		52.410	28.740	22.677		42.42	6
	ATOM	904	OH	TYR A	113	52.008	29.952	23.211		42.79	8

WO 01/58951	PCT/EP01/01457

						-87				
	ATOM	905	С	TYR A	113	55.097	24.250	22.936	1.00 47.38	6
	ATOM	906	Ō	TYR A		54.304	23.508	23.506	1.00 47.08	8
	ATOM	907	N	MET A		56.047	24.916	23.577	1.00 48.38	7
	ATOM	908	CA	MET A		56.205	24.788	25.015	1.00 48.39	6
5	ATOM	909	CB	MET A		57.485	24.020	25.304	1.00 52.09	6
	MOTA	910	CG	MET A	114	57.675	23.679	26.739	1.00 59.10	· 6
	ATOM	911	SD	MET A	114	59.383	23,282	26.925	1.00 67,20	16
	MOTA	912	CE	MET A	114	59.324	21.518	26.416	1.00 67.26	6
	ATOM	913	С	MET A		56.245	26.148	25.701	1.00 46.12	6
10	ATOM	914	0	MET A	114	57.308	26.660	26.027	1.00 46.76	8
	ATOM	915	N	PRO A	115	55.076	26.754	25.922	1.00 44.80	7
	ATOM	916	CD	PRO A	115	53.740	26.329	25.463	1.00 44.54	6
	ATOM	917	CA	PRO A	115	55.005	28.059	26.575	1.00 44.08	6
	MOTA	918	CB	PRO A	115	53.675	28.598	26.075	1.00 45.01	6
15	MOTA	919	CG	PRO A	115	52.831	27.366	26.077	1.00 43.44	6
	ATOM	920	С	PRO A	115	55.030	27.935	28.102	1.00 43.24	6
	MOTA	921	0	PRO A	115	54.552	26.947	28.664	1.00 40.79	8
	MOTA	922	N	SER A	116	55.599	28.929	28.771	1.00 42.36	7
	MOTA	923	CA	SER A	116	55.627	28.911	30.227	1.00 42.64	6
20	MOTA	924	CB	SER A	116	56.851	29.624	30.764	1.00 40.99	6
	MOTA	925	OG	SER A	116	56.852	29.573	32.169	1.00 41.56	8
	ATOM	926	С	SER A	116	54.382	29.658	30.653	1.00 42.71	6
	ATOM	927	0	SER A	116	54.184	30.809	30.266	1.00 44.52	8
05	MOTA	928	N	ILE A		53.545	29.006	31.446	1.00 41.18	7
25	ATOM	929	CA	ILE A		52.303	29.616	31.879	1.00 40.12	6
	MOTA	930	CB	ILE A		51.104	28.814	31.325	1.00 37.67	6
	MOTA	931	CG2	ILE A		49.805	29.400	31.819	1.00 38.25	6
	ATOM	932	CG1	ILE A		51.134	28.825	29.798	1.00 36.76	6
00	MOTA	933		ILE A		50.212	27.822	29.169	1.00 33.48	6
30	MOTA	934	C	ILE A		52.114	29.768	33.388	1.00 41.31	6
	ATOM	935	0	ILE A		52.444	28.876	34.168	1.00 43.78	8
	MOTA	936	N	ARG A		51.607	30.925	33.795	1.00 41.35	
	ATOM	937	CA	ARG A		51.283	31.153	35.194	1.00 41.26	6
35	MOTA	938	CB	ARG A		51.789	32.496	35.709	1.00 38.56	6
33	MOTA	939	CG	ARG A		51.290	32.758	37.113	1.00 37.29	6
	MOTA MOTA	940 941	CD	ARG A		52.006	33.883	37.817	1.00 38.24	6
	ATOM	941	NE CZ	ARG A		51.453	34.066	39.150	1.00 41.49	7
	ATOM	943		ARG A	_	52.006 53.148	34.794	40.107	1.00 43.10 1.00 46.98	6 7
40	ATOM	944		ARG A		51.417	35.423 34.890	39.892 41.282	1.00 43.38	7
40	MOTA	945	C	ARG A		49.765	31.156	35.179	1.00 43.21	6
	MOTA	946	Ö	ARG A		49.144	31.842	34.374	1.00 41.21	8
	MOTA	947	N	GLN A		49.152			1.00 41.94	
	ATOM	948	CA	GLN A		47.702	30.329	36.056	1.00 43.44	
45	ATOM	949	CB	GLN A		47.292	29.433	34.895	1.00 41.21	6
	MOTA	950	CG	GLN A		45.825	29.257	34.672	1.00 43.47	6
	ATOM	951	CD	GLN . A		45.552	28.554	33.364	1.00 41.25	6
	MOTA	952	OE1			46.333	27.721	32.931	1.00 42.28	8
	MOTA	953	NE2	GLN A		44.439	28.877	32.736	1.00 42.81	7
50	MOTA	954	С	GLN A	119	47.183	29.801	37.385	1.00 44.09	6
	MOTA	955	0	GLN A	119	47.866	29.041	38.062	1.00 43.59	8
	MOTA	956	N	ARG A	120	45.990	30.228	37.778	1.00 46.26	7
	MOTA	957	CA	ARG A	120	45.433	29.762	39.036	1.00 48.60	6
	MOTA	958	CB	ARG A		44.780	30.900	39.797	1.00 51.27	6
55·	MOTA	959	CG	ARG A	120	45.705	32.036	40.096	1.00 60.62	6
	MOTA	960	CD	ARG A		45.261	32.728	41.362	1.00 67.20	6
	ATOM	961	NE	ARG A		45.730	32.045	42.575	1.00 69.70	7
	ATOM	962	CZ	ARG A		44.989	31.859	43.668	1.00 69.76	6
00	ATOM	963		ARG A		43.728	32.279	43.709	1.00 68.36	7
60	ATOM	964		ARG A		45.533	31.307	44.748	1.00 70.33	7
	ATOM	965	С	ARG A	120	44.414	28.669	38.804	1.00 48.02	6

						-88				
	ATOM	966	0 7	ARG A	120	43.706	28.669	37.788	1.00 46.40	8
	ATOM	967	-	PHE A		44.341	27.739	39.753	1.00 46.74	7
	ATOM	968		PHE A		43.406	26.628	39.648	1.00 48.15	6
	ATOM	969		PHE A		44.129	25.330	39.301	1.00 45.72	6
5	ATOM	970		PHE A		44.973	25.415	38.074	1.00 44.95	6
9	ATOM	971		PHE A		46.240	25.993	38.122	1.00 43.54	٠6
	ATOM	972		PHE A		44.495	24.944	36.866	1.00 41.66	6
		973		PHE A		47.011	26.099	36.986	1.00 42.05	6
	MOTA	974		PHE A		45.257	25.047	35.733	1.00 41.56	6
10	ATOM	975		PHE A		46.521	25.628	35.790	1.00 42.24	6
١Ģ	ATOM	976		PHE A		42.622	26.376	40.908	1.00 49.43	6
	ATOM	977		PHE A		42.996	26.810	42.001	1.00 49.47	8
	ATOM	978	-	SER A		41.524	25.653	40.727	1.00 51.17	7
•	ATOM	979		SER A		40.657	25.250	41.823	1.00 52.06	6
15	MOTA	980		SER A		39.193	25.501	41.477	1.00 52.69	6
10	ATOM	981		SER A		38.354	25.046	42.520	.1.00 51.12	8
	ATOM	982	C	SER A		40.896	23.754	41.978	1.00 52.70	6
	MOTA	983	ō	SER A		40.529	22.966	41.103	1.00 51.13	8
	MOTA	984	N	CYS A		41.543	23.369	43.070	1.00 52.97	7
20	MOTA	985	CA	CYS A		41.820	21.967	43.312	1.00 56.03	6
_0	ATOM	986	C	CYS A		42.017	21.693	44.803	1.00 59.48	6
	ATOM	987	ō	CYS A		41.882	22.602	45.634	1.00 60.13	8
	ATOM	988	СВ	CYS A		43.052	21.555	42.534	1.00 53.78	6
	ATOM	989	SG	CYS A		44.483	22.558	42.968	1.00 56.89	16
25	ATOM	990	N	ASP A		42.342	20.443	45.143	1.00 61.91	7
	ATOM	991	CA	ASP A		42.525	20.084	46.542	1.00 63.81	6
	ATOM	992	СВ	ASP A		42.391	18.571	46.749	1.00 65.05	6
	MOTA	993	CG	ASP A	124	41.828	18.226	48.128	1.00 66.74	6
	ATOM	994	OD1	ASP A	124	42.113	18.973	49.103	1.00 65.03	8
30	ATOM	995	OD2	ASP A	124	41.101	17.209	48.234	1.00 67.39	8
	MOTA	996	С	ASP A	. 124	43.857	20.543	47.110	1.00 63.72	6
	MOTA	997	0	ASP A	124	44.910	20.036	46.745	1.00 64.11	8
	MOTA	998	N	VAL A	125	43.794	21.495	48.031	1.00 64.49	7
	MOTA	999	CA	VAL A		44.981	22.042	48.681	1.00 63.28	6
35	ATOM	1000	CB	VAL A		44.861	23.578	48.804	1.00 62.29	6
	MOTA	1001		VAL A		46.058	24.135	49.539	1.00 61.76	
	MOTA	1002	CG2	VAL A		44.735	24.194	47.429	1.00 61.51	6 6
	MOTA	1003	С	VAL A		45.190	21.449	50.078	1.00 63.42	8
	MOTA	1004	0	VAL A		46.283	21.534	50.632	1.00 63.08 1.00 64.34	7
40	MOTA	1005	N	SER A		44.141	20.848	50.641		6
	MOTA	1006	CA	SER F		44.218	20.252			6
	MOTA	1007	CB	SER A		42.924	19.503		1.00 58.95	8
	MOTA	1008	OG	SER A		42.723	18.465			6
	MOTA	1009		SER A		45.414	19.306			8
45	MOTA	1010			A 126	45.636	18.420		_	7
	MOTA	1011			A 127	46.188	19.510			6
	MOTA	1012			A 127	47.343	18.676			6
	MOTA	1013			A 127	48.647				8
	MOTA	1014		GLY A	A 127	49.725				7
50	MOTA	1015			A 128	48.572				6
	MOTA	1016			A 128	49.779 49.505				6
	MOTA	1017			A 128	.48.855		_		6
	MOTA	1018		1 VAL .		48.625				6
<b>~</b> ~	MOTA	1019		VAL.	A 128 A 128	50.792				6
55	MOTA	1020			A 128	51.984				8
	MOTA	1021			A 128 A 129	50.324				7
	MOTA	1022			A 129 A 129	51.241				6
	MOTA	1023			A 129 A 129	50.507			_	6
60	MOTA	1024			A 129 A 129	51.427				
60	MOTA	1025 1026		1 ASP		51.000				
	MOTA	102	ريب د			J <b>v</b> .				

	WO 01/58	3951							PCT/EP01/01	457
						-89				
	MOTA	1027	OD2	ASP 2	129	52.578	23.546	57.311	1.00 80.59	8
	ATOM	1028	C		A 129	52.085	21.164	55.676	1.00 80.77	6
	MOTA	1029	0		A 129	53.089	21.441	56.355	1.00 80.25	8
_	MOTA	1030	N		4·130	51.724	19.907	55.389	1.00 80.58	7
5	MOTA	1031	CA		A 130	52.541	18.824	55.925	1.00 81.44	6
	ATOM	1032	CB		A 130	52.508	18.858	57.465	1.00 83.89 1.00 85.49	6
	MOTA MOTA	1033 1034		THR I		51.433 · 53.882	19.722 19.331	57.880 58.047	1.00 83.49	8 6
	ATOM	1035	C		A 130	52.309	17.374	55.529	1.00 80.12	6
10	ATOM	1036	ō		A 130	51.199	16.974	55.148	1.00 78.43	8
	MOTA	1037	N	GLU .	A 131	53.404	16.611	55.654	1.00 79.90	7
	MOTA	1038	CA		A 131	53.459	15.165	55.432	1.00 80.19	6
	MOTA	1039	CB		A 131	52.364	14.489	56.272	1.00 82.93	6
15	MOTA	1040 1041	CG		A 131	52.693 51.440	14.372	57.760·	1.00 86.59 1.00 88.67	6 6
15	ATOM ATOM	1041	CD OE1	GLU .	A 131 A 131	50.524	14.289 13.470	58.632 58.311	1.00 88.67	8
	MOTA	1043		GLU .		51.380	15.050	59.638	1.00 88.79	8
	ATOM	1044	C		A 131	53.378	14.637	54.012	1.00 79.05	6
	MOTA	1045	0	GLU 2	A 131	54.337	14.716	53.231	1.00 77.86	8
20	ATOM	1046	N		A 132	52.227	14.033	53.727	1.00 77.68	7
	MOTA	1047	CA		A 132	51.915	13.474	52.426	1.00 76.46	6
	ATOM ATOM	1048 1049	CB OG		A 132 A 132	50.796 49.642	12.429 12.990	52.576 53.176	1.00 76.05 1.00 74.46	6 8
	ATOM	1050	C		A 132	51.462	14.653	51.533	1.00 74.40	6
25	MOTA	1051	Ö		A 132	51.123	14.479	50.355	1.00 75.58	8
	MOTA	1052	N	GLY .	A 133	51.468	15.848	52.127	1.00 73.94	7
	ATOM	1053	CA		A 133	51.094	17.056	51.421	1.00 71.52	6
	MOTA	1054	C		A 133	49.754	16.971	50.735	1.00 70.11	6
30	ATOM ATOM	1055 1056	O		A 133 A 134	48.927 49.540	16.115 17.864	51.060 49.774	1.00 69.95 1.00 68.35	8 7
30	ATOM	1056	N CA		A 134	48.290	17.895	49.774	1.00 65.73	6
	ATOM	1058	СВ		A 134	47.748	19.321	48.982	1.00 65.87	6
	MOTA	1059	С		A 134	48.476	17.359	47.621	1.00 63.96	6
0-	MOTA	1060	0		A 134	49.600	17.219	47.124	1.00 61.93	8
35	MOTA	1061	N		A 135	47.353	17.048	46.985	1.00 63.38	7
	MOTA	1062	CA CB		A 135 A 135	47.359	16.549	45.621	1.00 62.44 1.00 62.52	6 6
	MOTA MOTA	1063 1064		THR		47.003 47.951	15.066 14.323	45.562 46.345	1.00 62.32	8
	ATOM	1065	CG2		A 135	47.040	14.574	44.122	1.00 61.31	6
40	ATOM	1066	C		A 135	46.350	17.355	44.820	1.00 61.68	6
	MOTA	1067	0		A 135	45.120	17.188	44.944	1.00 60.36	8
	MOTA	1068	N		A 136	46.900	18.259	44.017	1.00 59.30	7
	MOTA	1069	CA		A 136	46.115	19.129	43.178	1.00 56.11	6
45	MOTA MOTA	1070 1071	C C		A 136 A 136	46.111 47.168	18.538 18.370	41.778 41.163	1.00 55.58 1.00 53.10	6 8
.0	ATOM	1072	CB		A 136	46.739	20.518	43.181	1.00 55.44	6
	MOTA	1073	SG		A 136	46.010	21.663	41.978	1.00 54.51	16
	MOTA	1074	N		A 137	44.917	18.191	41.298	1.00 55.48	7 .
<b>5</b> 0	MOTA	1075	CA		A 137	44.764	17.611	39.968	1.00 56.07	6
50	ATOM	1076	CB		A 137	43.786	16.431	39.990	1.00 58.27	6
	MOTA	1077	CG		A 137 A 137	44.213 43.017	15.318 14.517	40.915	1.00 62.94 1.00 67.01	6
	MOTA MOTA	1078 1079	CD NE		A 137	43.017	13.821	41.384 42.641	1.00 72.70	6 7
	ATOM	1080	CZ		A 137	44.131	12.772	42.762	1.00 74.69	6
55	MOTA	1081		ARG		44.765	12.270	41.696	1.00 74.12	7
	ATOM	1082	NH2	ARG	A 137	44.326	12.226	43.958	1.00 74.27	7
	ATOM	1083	C		A 137	44.265	18.670	39.010	1.00 53.72	6
	ATOM	1084	0		A 137	43.325	19.396	39.301	1.00 51.52	. 8
60	MOTA MOTA	1085 1086	N CA		A 138 A 138	44.917 44.582	18.738 19.696	37.860 36.825	1.00 52.05 1.00 50.25	· 7
30	ATOM	1083	CB		A 138	45.778	20.624	36.557	1.00 49.78	6
					_	<del>_</del>	_		· · · <del>-</del>	_

						-90				
	ATOM	1088	CG2	ILE A	138	45.449	21.566	35.421	1.00 48.31	6
	ATOM	1089		ILE A		46.150	21,389	37.837	1.00 48.07	6
	ATOM	1090		ILE A		47.444	22.144	37.750	1.00 41.58	6
	MOTA	1091		ILE A		44.270	18.925	35.555	1.00 49.76	6
5	ATOM	1092	ō	ILE A		45.119	18.190	35.058	1.00 50.40	8
•	ATOM	1093		LYS A		43.059	19.081	35.032	1.00 49.44	. 7
	ATOM	1094		LYS A		42.672	18.374	33.809	1.00 51.81	6
	ATOM	1095		LYS A		41.285	17.713	33.969	1.00 52.86	6
	ATOM	1096		LYS A		41.176	16.772	35.164	1.00 56.41	6
10	ATOM	1097		LYS A		39.919	15.940	35.137	1.00 57.01	6
	ATOM	1098		LYS A		39.978	14.888	34.047	1.00 60.31	6
	ATOM	1099	NZ	LYS A		38.728	14.066	33.965	1.00 59.02	7
	MOTA	1100	С	LYS A	139	42.628	19.317	32.615	1.00 51.20	6
	ATOM	1101	0	LYS A	139	41.964	20.340	32.673	1.00 51.87	8
15	ATOM	1102	N	ILE A		43.325	18.979	31.535	1.00 49.23	7
	ATOM	1103	CA	ILE A	140	43.295	19.826	30.354	1.00 49.38	6
	MOTA	1104	CB	ILE A	140	44.578	20.710	30.278	1.00 50.36	6
	MOTA	1105	CG2	ILE A	140	44.889	21.277	31.653	1.00 51.45	6
	MOTA	1106	CG1	ILE A	140	45.794	19.900	29.868	1.00 50.82	6
20	MOTA	1107	CD1	ILE A	140	47.103	20.630	30.148	1.00 51.49	6
	ATOM	1108	С	ILE A	140	43.088	19.025	29.066	1.00 47.91	6
	ATOM	1109	0	ILE A	140	43.721	18.006	28.859	1.00 46.67	8
	MOTA	1110	N	GLY A	141	42.168	19.485	28.220	1.00 48.53	7
	MOTA	1111	CA	GLY A	141	41.885	18.811	26.959	1.00 47.60	6
25	MOTA	1112	С	GLY A	141	41.255	19.765	25.958	1.00 48.49	6
	ATOM	1113	0	GLY A	141	40.938	20.900	26.317	1.00 49.03	8
	MOTA	1114	N	SER A	142	41.070	19.329	24.712	1.00 46.01	7
	MOTA	1115	CA	SER A	142	40.466	20.195	23.699	1.00 43.95	6
	MOTA	1116	CB	SER A	142	40.306	19.466	22.370	1.00 44.36	6
30	ATOM	1117	OG	SER A		39.494	20.214	21.477	1.00 39.73	8
	MOTA	1118	C	SER A		39.107	20.686	24.144	1.00 45.09	6
	ATOM	1119	0	SER A		38.319	19.934	24.714	1.00 47.13	8
	MOTA	1120	N	TRP A		38.822	21.947	23.862	1.00 43.97	7
۰-	MOTA	1121	CA	TRP A		37.564	22.537	24.256	1.00 41.28	6
35	ATOM	1122	CB	TRP A		37.754	24.033	24.473	1.00 42.28	6
	MOTA	1123	CG	TRP A		36.577	24.697	25.126	1.00 42.52	6
	MOTA	1124		TRP A		36.215	24.610	26.505	1.00 39.43	6
	MOTA	1125	CE2	TRP A		35.025	25.359	26.676	1.00 39.15	6
40	ATOM	1126		TRP A		36.778	23.969	27.613	1.00 37.16	6
40	ATOM	1127		TRP A		35.618	25.480	24.526	1.00 41.93	6 7
	ATOM	1128		TRP A		34.681	25.880	25.456	1.00 40.50 1.00 39.06	6
	ATOM	1129		TRP A		34.393	25.480 24.090	27.911 28.837	1.00 39.00	6
	ATOM	1130		TRP A		36.150	24.840	28.978	1.00 39.37	6
45	MOTA	1131 1132		TRP A		34.968 36.450	22.307	23.258	1.00 33.40	6
40	MOTA		C	TRP A		35.287	22.307	23.236	1.00 42.45	8
	MOTA MOTA	1133 1134	O N	THR A		36.790	22.239	21.983	1.00 42.43	7
	ATOM	1134	CA	THR A		35.760	21.992	20.979	1.00 41.13	6
	ATOM	1136	CB	THR A		35.703	23.191	20.051	1.00 39.00	6
50	MOTA	1137		THR A		36.994	23.416	19.490	1.00 39.19	8
00	ATOM	1138		THR A		35.288	24.420	20.818	1.00 37.78	6
	MOTA	1139	C	THR A		35.879	20,738	20.148	1.00 42.54	6
	ATOM	1140	Ö	THR A		34.941	20.385	19.443	1.00 45.82	8
	ATOM	1141	N	HIS A		37.012	20.054	20.233	1.00 43.18	7
55	ATOM	1142	CA	HIS A		37.187	18.837	19.459	1.00 46.20	6
	ATOM	1143	CB	HIS A		38.517	18.875	18.707	1.00 46.05	6
	ATOM	1144	CG	HIS A		38.588	19.933	17.646	1.00 46.56	6
	ATOM	1145		HIS A		37.994	20.022	16.432	1.00 45.44	6
	ATOM	1146		HIS A		39.366	21.061	17.772	1.00 44.61	7
60	ATOM	1147	CE1	HIS A	145	39.250		16.682	1.00 43.87	6
	ATOM	1148	NE2	HIS A	145	38.423	21.189	15.853	1.00 41.35	7

						-91				
	ATOM	1149	С	HIS A	145	37.105	17.570	20.303	1.00 47.36	6
	MOTA	1150		HIS A		37.811	17.422	21.298	1.00 47.71	8
	ATOM	1151	N	HIS A	146	36.230	16.656	19.898	1.00 48.75	7
	ATOM	1152	CA	HIS A	146	36.067	15.400	20.609	1.00 50.47	6
5	MOTA	1153	CB	HIS A	146	34.658	14.846	20.365	1.00 49.28	6
	MOTA	1154	CG	HIS A	146	34.314	14.694	18.919	1.00 50.42	· 6
	ATOM	1155	CD2	HIS A	146	34.954	14.057	17.910	1.00 50.68	6
	ATOM	1156		HIS A		33.183	15.248	18.362	1.00 51.90	7
	ATOM	1157	CE1	HIS A	146	33.138	14.962	17.073	1.00 49.57	6
10	MOTA	1158	NE2	HIS A	146	34.202	14.239	16.774	1.00 51.03	7
	ATOM	1159	С	HIS A	146	37.137	14.396	20.167	1.00 49.74	6
	ATOM	1160	0	HIS A	146	37.927	14.673	19.268	1.00 49.87	8
	ATOM	1161	N	SER A	147	37.145	13.234	20.809	1.00 50.23	7
	ATOM	1162	CA	SER A	147	38.101	12.158	20.543	1.00 50.98	6
15	MOTA	1163	CB	SER A	147	37.722	10.934	21.372	1.00 50.73	6
	MOTA	1164	OG	SER A	147	36.346	10.642	21.240	1.00 51.84	8
	MOTA	1165	С	SER A	147	38.314	11.730	19.096	1.00 51.53	6
	MOTA	1166	0	SER A	147	39.374	11.228	18.754	1.00 50.53	8
	MOTA	1167	N	ARG A	148	37.319	11.925	18.245	1.00 53.75	7
20	MOTA	1168	CA	ARG A		37.444	11.528	16.850	1.00 56.68	6
	MOTA	1169	CB	ARG A		36.052	11.408	16.221	1.00 60.77	6
	MOTA	1170	CG	ARG A		35.100	10.487	16.985	1.00 70.28	6
	MOTA	1171	CD	ARG A		33.673	10.516	16.423	1.00 76.18	6
	MOTA	1172	NE	ARG A		32.702	9.919	17.351	1.00 83.11	7
25	MOTA	1173	$\mathbf{cz}$	ARG A		32.685	8.632	17.719	1.00 85.65	6
	ATOM	1174	NH1	ARG A		33.595	7.781	17.243	1.00 86.70	7
,	MOTA	1175		ARG A		31.746	8.187	18.549	1.00 85.60	7
	MOTA	1176	C	ARG A		38.295	12.502	16.025	1.00 56.73	6
20	MOTA	1177	0	ARG A		38.774	12.157	14.938	1.00 56.48	8 7
30	MOTA	1178	N	GLU A		38.477	13.714	16.553	1.00 55.77	
	MOTA	1179	CA	GLU A		39.233	14.767	15.884	1.00 51.96 1.00 52.02	6 6
	MOTA	1180	CB	GLU A		38.384	16.037 15.748	15.821 15.527	1.00 52.02	6
	MOTA	1181	CG	GLU A		36.918 36.065	16.989	15.327	1.00 49.98	6
35	MOTA	1182 1183	CD OF1	GLU A		36.220	17.879	16.273	1.00 49.58	8
00	MOTA MOTA	1184	OE1	GLU A		35.226	17.070	14.506	1.00 46.84	8
	MOTA	1185	C	GLU A		40.531	15.030	16.627	1.00 50.15	6
	MOTA	1186	0	GLU A		41.584	15.167	16.013	1.00 49.33	8
	ATOM	1187	Ν.	ILE A		40.454	15.100	17.950	1.00 47.25	7
40	ATOM	1188	CA	ILE A		41.643	15.309	18.748	1.00 48.44	6
	ATOM	1189	CB	ILE A		41.712	16.740	19.374	1.00 48.83	6
	ATOM	1190		ILE A		42.759	16.793	20.481	1.00 44.42	6
	MOTA	1191		ILE A	4-6	42.104	17.769	18.316	1.00 49.22	6
	ATOM	1192		ILE A		42.185	19.175	18.839	1.00 45.68	6
45	ATOM	1193	С	ILE A		41.707	14.310	19.881	1.00 50.37	6
	ATOM	1194	0	ILE A		40.712	14.031	20.536	1.00 50.37	8
	MOTA	1195	N	SER A	151	42.902	13.781	20.104	1.00 52.48	7
	ATOM	1196	CA	SER A	151	43.156	12.841	21.178	1.00 54.49	6
	MOTA	1197	CB	SER A	. 151	43.437	11.452	20.611	1.00 54.22	6
50	MOTA	1198	OG	SER A	151	44.619	11.457	19.844	1.00 54.28	8
	ATOM	1199	С	SER I		44.385	13.381	21.899	1.00 55.57	6
	MOTA	1200	0	SER A		45.347	13.798	21.257	1.00 56.29	8
	MOTA	1201	N	VAL A		44.337	13.400	23.227	1.00 57.03	7
	ATOM	1202	CA	VAL A		45.447	13.897	24.033	1.00 59.85	6
55	MOTA	1203	CB	VAL A		44.979	14.922	25.100	1.00 59.80	6
	MOTA	1204		VAL A		44.170	16.021	24.447	1.00 60.14	6
	MOTA	1205		VAL A		44.163	14.225	26.175	1.00 61.09	6
	MOTA	1206	C	VAL A		46.084	12.722	24.747	1.00 61.00	6
60	MOTA	1207	0	VAL A		45.393	11.785	25.132	1.00 59.83	8
60	MOTA	1208	N	ASP A		47.398	12.780	24.932	1.00 63.57	7
	MOTA	1209	CA	ASP A	7 723	48.114	11.690	25.582	1.00 66.72	6

							-92				
	ATOM	1210	СВ	ASP A	A 1	53	48.620	10.724	24.505	1.00 66.16	6
	ATOM	1211		ASP A			47.505	10.245	23.573	1.00 67.72	6
	ATOM	1212		ASP A			46.769°	9.317	23.972	1.00 68.96	8
	ATOM	1213		ASP Z			47.354	10.801	22.451	1.00 67.60	8
5	MOTA	1214	C	ASP Z	A 1	53	49.293	12.198	26.422	1.00 68.93	6
	MOTA	1215	0	ASP A	A 1	53	49.951	13.175	26.058	1.00 69.39	8
	ATOM	1216	N	PRO 2	A 1	54	49.553	11.564	27.577	1.00 70.74	7
	MOTA	1217	CD	PRO J	A 1	54	48.601	10.759	28.357	1.00 71.40	6
	ATOM	1218	CA	PRO 2	A 1	54	50.675	11.995	28.421	1.00 73.42	6
10	ATOM	1219	CB	PRO 2	A 1	54	50.421	11.266	29.735	1.00 72.22	6
	ATOM	1220	CG	PRO 2	A 1	54	48.930	11.182	29.776	1.00 72.97	6
	ATOM	1221	С	PRO I	A 1	54	51.999	11.580	27.773	1.00 75.99	6
	MOTA	1222	0	PRO .	A 1	54	51.997	10.951	26.716	1.00 75.49	8
	MOTA	1223	N	THR .			53.121	11.916	28.406	1.00 79.97	7
15	MOTA	1224	CA	THR .			54.433	11.580	27.851	1.00 84.54	6
	MOTA	1225	CB	THR .			55.002	12.797	27.084	1.00 84.38	6
	MOTA	1226		THR			55.314	13.844	28.015	1.00 85.24	8
	MOTA	1227	CG2	THR			53.979	13.326	26.085	1.00 83.86	6
00	MOTA	1228	C	THR			55.504	11.101	28.868	1.00.88.31	6 8
20	MOTA	1229	0	THR			55.179	10.480	29.905	1.00 89.23	7
	MOTA	1230	N	THR			56.774	11.402 11.057	28.539 29.337	1.00 91.22	6
	MOTA	1231	CA	THR			57.970 50.146	12.041	29.337	1.00 93.80	6
	ATOM	1232	CB	THR			59.146 59.430	12.041	27.631	1.00 93.55	8
25	MOTA	1233	OG1	THR THR			60.414	11.624	29.839	1.00 93.12	6
25	MOTA	1234	CG2 C	THR			57.778	11.024	30.862	1.00 95.49	6
	ATOM ATOM	1235 1236	0	THR			57.812	12.080	31.532	1.00 95.50	8
	MOTA	1237	N	GLU			57.614	9.827	31.406	1.00 97.12	7
	ATOM	1238	CA	GLU			57.411	9.649	32.841	1.00 98.24	6
30	ATOM	1239	CB	GLU			56.619	8.370	33.095	1.00100.23	6
-	MOTA	1240	CG	GLU			55.476	8.150	32.109	1.00103.23	6
	ATOM	1241	CD	GLU			54.728	6.842	32.372	1.00104.38	6
	ATOM	1242	OE1	GLU	A 1	L57	55.391	5.769	32.462	1.00103.49	8
	MOTA	1243	OE2	GLU	A 3	L57	53.475	6.896	32.482	1.00105.11	8
35	MOTA	1244	С	GLU			58.731	9.570	33.591	1.00 98.22	6
	MOTA	1245	0	GLU			58.742	9.488	34.825	1.00 98.77	8
	MOTA	1246	N	ASN			59.840	9.582	32.854	1.00 97.95	7
	MOTA	1247	CA	ASN			61.154	9.505	33.494	1.00 98.34	6
40	MOTA	1248	CB	ASN			62.244	9.212	32,455	1.00100.52 1.00102.32	6 6
40	MOTA	1249	CG	ASN			61.953	7.969 6.872	31.634	1.00102.32	8
	MOTA	1250		ASN			61.787 61.898	8.131	32.184 30.305	1.00104.10	7
	MOTA	1251		ASN				10.832			6
	MOTA	1252	C	ASN ASN			61.170	11.019	35.392	1.00 96.34	8
45	MOTA MOTA	1253 1254	O N	SER			62.093	11.729	33.423	1.00 94.95	7
40	ATOM	1255	CA	SER			62.492	13.069	33.857	1.00 91.51	6
	ATOM	1256	СВ	SER			61.878	14.091	32.890	1.00 91.99	6
	ATOM	1257	OG	SER			60.550	13.708	32.529	1.00 90.83	8
	ATOM	1258	C	SER			62.116	13.412	35.301	1.00 88.77	6
50	MOTA	1259	. 0	SER			60.939	13.380	35.666	1.00 88.38	8
	MOTA	1260	N	ASP			63.120	13.728	36.120	1.00 85.60	7
	MOTA	1261	CA	ASP	A :	160	62.867	14.093	37.517	1.00 81.69	6
	MOTA	1262	CB	ASP	A :	160	64.107	14.716	38.164	1.00 81.79	6
	MOTA	1263	CG	ASP			63.827	15.217	39.578	1.00 82.16	6
55	MOTA	1264		. ASP			64.609	16.057	40.075	1.00 82.93	8
	MOTA	1265		ASP			62.824	14.766	40.194	1.00 81.33	8
	MOTA	1266	С	ASP			61.748	15.125	37.556	1.00 78.87 1.00 77.29	6 8
	MOTA	1267	0	ASP			61.906 60.643	16.215 14.783	36.997 38.223	1.00 77.29	7
60	MOTA	1268	N CA	ASP ASP			59.493	15.677	38.324	1.00 73.12	6
JU	MOTA MOTA	1269 1270	CB	ASP			58.433	15.111	39.273	1.00 71.12	6
	AION	12/0	CD				30.133	<b>_</b>			-

	WO 01/58	951					PCT/EP01/0	1457		
						-93				
	ATOM	1271	CG	ASP A	161	57.719	13.895	38.698	1.00 71.43	6
•	ATOM	1272		ASP A		57.509	13.854	37.463	1.00 70.50	
	ATOM	1273		ASP A		57.353	12.983	39.480	1.00 71.76	
	ATOM	1274	С	ASP A		59.814	17.097	38.756	1.00 69.97	
5	MOTA	1275	.0	ASP A		59.009	18.001	38.545	1.00 69.41	
	MOTA	1276	N	SER A	162	60.974	17.321	39.358	1.00 68.43	
	MOTA	1277	CA	SER A		61.282	18.682	39.774	1.00 68.46	
	ATOM	1278	CB	SER A		61.190	18.809	41.308	1.00 68 76	
10	MOTA	1279	OG	SER A		62.209	18.069	41.962	1.00 68.13	
10	MOTA	1280	G	SER A		62.636	19.163	39.289	1.00 67.78	
	ATOM ATOM	1281 1282	0	SER A		63.264	20.014	39.917 38.156	1.00 67.84 1.00 67.60	
	ATOM	1282	N CA	GLU A		63.087 64.382	18.640 19.052	37.649	1.00 67.80	
	ATOM	1284	CB	GLU A		64.884	18.051	36.609	1.00 70.48	
15	ATOM	1285	CG	GLU A		64.380	18.242	35.193	1.00 73.24	
	ATOM	1286	CD	GLU A		65.111	17.328	34.204	1.00 75.50	
	ATOM	1287	OE1			64.835	16.097	34.211	1.00 76.99	
	MOTA	1288	OE2	GLU A	163	65.970	17.842	33.438	1.00 73.24	
	MOTA	1289	C	GLU A	163	64.342	20.475	37.083	1.00 68.50	6
20	MOTA	1290	0	GLU A		65.385	21.062	36.774	1.00 69.29	
	ATOM	1291	N	TYR A		63.140	21.031	36.958	1.00 67.44	
	MOTA	1292	CA	TYR A		62.968	22.396	36.466	1.00 65.48	
	ATOM	1293	CB	TYR A		62.085	22.422	35.221	1.00 66.46	
25	ATOM	1294	CG	TYR A		62.709	21.754	34.029	1.00 67.50	
20	MOTA	1295		TYR A		62.082	20.664	33.415	1.00 68.14	
	ATOM ATOM	1296 1297	CE1 CD2	TYR A		62.664 63.942	20.011 22.185	32.328 33.527	1.00 67.68	
	ATOM	1298	CE2	TYR A		64.539	21.538	32.435	1.00 69.28	
	ATOM	1299	CZ	TYR A		63.892	20.449	31.837	1.00 68.44	
30	ATOM	1300	OH	TYR A		64.456	19.823	30.737	1.00 69.00	
••	ATOM	1301	C	TYR A		62.313	23.259	37.534	1.00 64.23	
	MOTA	1302	0	TYR A		62.181	24,474	37.368	1.00 62.7	
	MOTA	1303	N	PHE A		61.899	22.626	38.627	1.00 62.72	
	MOTA	1304	CA	PHE A	165	61.241	23.343	39.705	1.00 60.48	3 6
35	MOTA	1305	CB	PHE A		60.738	22.364	40.758	1.00 57.99	
	ATOM	1306	CG	PHE A		59.676	22.936	41.641	1.00 57.14	
	ATOM	1307		PHE A		58.424	23.252	41.115	1.00 55.84	
	MOTA	1308		PHE A		59.933	23.194	42.985	1.00 55.03	
40	MOTA	1309		PHE A		57.439	23.818	41.902	1.00 54.80	
70	MOTA MOTA	1310 1311	CEZ	PHE A		58.961 57.699	23.762 24.079	43.787 43.242	1.00 57.75	
	ATOM	1312	C	PHE A		62.159	24.369	40.354	1.00 60.44	
	ATOM	1313	ō	PHE A		63.348	24.121	40.547	1.00 60.7	
	ATOM	1314	N	SER A		61.611	25.534	40.676	1.00 60.9	
45	MOTA	1315	CA	SER A		62.418	26.567	41.312	1.00 61.13	
	MOTA	1316	CB	SER A	166	61.638	27.874	41.457	1.00 59.70	5 6
	MOTA	1317	OG	SER A	166	62.476	28.875	42.015	1.00 59.79	
	MOTA	1318	С	SER A		62.809	26.068	42.694	1.00 61.3	
-	ATOM	1319	0	SER A		62.009	25.442	43.393	1.00 61.62	
50	ATOM	1320	N	GLN A		64.038	26.359	43.089	1.00 61.83	
	MOTA	1321	CA	GLN A		64.525	25.931	44.393	1.00 62.17	_
	MOTA MOTA	1322 1323	CB CG	GLN A		66.052 -66.745	25.797 27.065	44.351 43.861	1.00 63.58	
	ATOM	1323	CD	GLN A		68.204	26.851	43.514	1.00 69.00	
55	ATOM	1325		GLN A		69.008	26.488	44.376	1.00 70.7	
	MOTA	1326	NE2	GLN A		68.556	27.081	42.241	1.00 69.2	
	MOTA	1327	C	GLN A		64.119	26.927	45.476	1.00 61.2	
	ATOM	1328	Ō	GLN A		64.112	26.585	46.659	1.00 61.1	
	ATOM	1329	N	TYR A		63.762	28.147	45.075	1.00 58.4	1 7
60	MOTA	1330	CA	TYR A		63.392	29.162	46.046	1.00 56.49	5 6
	MOTA	1331	СВ	TYR A	168	63.881	30.522	45.564	1.00 55.3	5 6

	WO 01/5	8951				PCT/EP01/01457					
						-94					
	MOTA	1332	CG	TYR A 16	8	65.335	30.469	45.158	1.00 57.58	6	
	MOTA	1333		TYR A 16			30.352	43.818	1.00 57.60	6	
	ATOM	1334		TYR A 16		67.031	30.233	43.439	1.00 57.86	6	
	ATOM	1335	CD2	TYR A 16	8	66.349	30.467	46.115	1.00 57.43	6	
5	ATOM	1336		TYR A 16		67.683 ·	30.347	45.749	1.00 58.19	6	
	ATOM	1337	CZ	TYR A 16	8	68.017	30.228	44.410	1.00 59.25	. 6	
	MOTA	1338	OH	TYR A 16	8	69.337	30.086	44.042	1.00 60.91	8	
	ATOM	1339	С	TYR A 16		61.912	29.199	46.383	1.00 56.00	6	
	MOTA	1340	0	TYR A 16		61.457	30.053	47.142	1.00 56.39	8	
10	MOTA	1341	N	SER A 16		61.162	28.257	45.832	1.00 55.67 1.00 56.31	7 6	
	MOTA	1342	CA	SER A 16		59.732	28.179	46.096	1.00 57.76	6	
	MOTA	1343	CB	SER A 16		59.082 57.699	27.123 26.971	45.197 45.501	1.00 57.76	8	
	ATOM	1344	OG	SER A 16		59.478	27.804	47.544	1.00 53.64	6	
15	MOTA	1345 1346	C 0	SER A 16		60.246	27.066	48.152	1.00 58.82	8	
13	MOTA MOTA	1347	N	ARG A 17		58.385	28.302	48.096	1.00 58.68	7	
	ATOM	1347	CA	ARG A 17		58.043	27.993	49.472	1.00 58.62	6	
	ATOM	1349	CB	ARG A 17		56.907	28.901	49.956	1.00 60.14	6	
	ATOM	1350	CG	ARG A 17		57.371	30.123	50.727	1.00 60.43	6	
20	ATOM	1351	CD	ARG A 17	70	56.401	31.291	50.589	1.00 64.30	6	
	ATOM	1352	NE	ARG A 17	70	55.020	30.998	50.989	1.00 66.31	7	
	ATOM	1353	CZ	ARG A 17		53.967	31.107	50.174	1.00 66.81	6	
	ATOM	1354		ARG A 17		54.129	31.489	48.915	1.00 63.97	7	
	MOTA	1355		ARG A 17		52.750	30.850	50.619	1.00 67.23	7	
25	ATOM	1356	С	ARG A 17		57.604	26.544	49.554	1.00 58.75 1.00 60.59	6 8	
	ATOM	1357	0	ARG A 17		57.516	25.975	50.642 48.405	1.00 50.39	7	
	MOTA	1358	N	PHE A 17		57.339 56.882	25.933 24.552	48.404	1.00 56.54	6	
	ATOM ATOM	1359 1360	CA CB	PHE A 17		55.499	24.479	47.765	1.00 55.41	6	
30	ATOM	1361	CG	PHE A 17		54.552	25.522	48.281	1.00 55.91	6	
00	ATOM	1362		PHE A 1		54.685	26.856	47.893	1.00 57.70	6	
	MOTA	1363		PHE A 17		53.560	25.190	49.203	1.00 56.28	6	
	MOTA	1364	CE1	PHE A 17	71	53.845	27.847	48.419	1.00 58.19	6	
	MOTA	1365	CE2	PHE A 1		52.718	26.170	49.732	1.00 55.91	6	
35	MOTA	1366	CZ	PHE A 1		52.864	27.505	49.337	1.00 57.16	6	
	MOTA	1367	C	PHE A 1		57.844	23.612	47.695	1.00 56.77 1.00 56.03	6 8	
	MOTA	1368	0	PHE A 1		58.841	24.045 22.319	47.113 47.765	1.00 56.03	7	
	MOTA	1369	N	GLU A 1'		57.552 58.389	22.319	47.703	1.00 58.00	6	
40	MOTA MOTA	1370	CA CB	GLU A 1		59.371	20.707	48.119	1.00 60.23	6	
+0	ATOM	1371 1372	CG	GLU A 1		58.734	19.970	49.303	1.00 64.00	6	
	MOTA	1373	CD	GLU A 1		59.769	19.445	50.313	1.00 66.01	6	
	MOTA	1374		GLU A 1		60.869	19.042	49.868	1.00 69.59	8	
	MOTA	1375		GLU A 1		59.487	19.421	51.541	1.00 65.33	8	
45	MOTA	1376	С	GLU A 1	72	57.497	20.259	46.518	1.00 59.67	. 6	
	MOTA	1377	0	GLU A 1	72	56.356	20.064	46.955	1.00 60.12	8	
	MOTA	1378	N	ILE A 1		58.006	19.579	45.496	1.00 60.16	7	
	MOTA	1379	CA	ILE A 1		57.224	18.545	44.827	1.00 60.67	6	
	MOTA	1380	CB	ILE A 1		57.413	18.587	43.291	1.00 61.87	6 6	
50	ATOM	1381		LILE A 1		56.659	17.422	42.644 42.727	1.00 62.56 1.00 61.03	6	
	ATOM	1382		ILE A 1		56.920 57.165	19.919 20.062	41.244	1.00 59.49	6	
	MOTA	1383	CDI	ILE A 1 ILE A 1		.57.579	17.150	45.296	1.00 59.83	6	
	MOTA MOTA	1384 1385	0	ILE A 1		58.751	16.770	45.360	1.00 57.21	8	
55	ATOM	1386	Ŋ	LEU A 1		56.554	16.381	45.616	1.00 61.63	7	
50	MOTA	1387	CA	LEU A 1		56.786	15.022	46.056	1.00 64.20	6	
	MOTA	1388	CB	LEU A 1		55.687	14.592	47.024	1.00 63.47	6	
	ATOM	1389	CG	LEU A 1	74	55.461	15.601	48.149	1.00 65.34	6	
	MOTA	1390		L LEU A 1	.74	54.285	15.144	49.024	1.00 66.19	6	
60	MOTA	1391		LEU A 1		56.747	15.770	48.962	1.00 64.00	6	
	MOTA	1392	С	LEU A 1	.74	56.783	14.147	44.806	1.00 65.92	6	

						-95					
	ATOM	1393	0	LEU A	174	57.757	13.440	44.522	1.00 65	. 29	8
	ATOM	1394		ASP A			14.233	44.036	1.00 67	. 33	7
	ATOM	1395		ASP A			13.436	42.827	1.00 68	.45	6
	ATOM	1396		ASP A		55.227	11.993	43.223	1.00 68	.56	6
5	ATOM	1397		ASP A		55.161	11.038	42.032	1.00 68		6
•	ATOM	1398		ASP A		56.141	10.964	41.244	1.00 67		8
	MOTA	1399		ASP A		54.121	10.347	41.905	1.00 67		8
	ATOM	1400		ASP A		54.542	14.023	41.872	1.00 69		6
	ATOM	1401		ASP A	175	53.617	14.735	42.286	1.00 69		8
10	ATOM	1402		VAL A		54.714	13.727	40.587	1.00 68		7
	ATOM	1403		VAL A		53.809	14.198	39.552	1.00 67		6
	ATOM	1404	CB	VAL A		54.461	15.324	38.694	1.00 67		6
	ATOM	1405	CG1	VAL A	176	53.533	15.721	37.542	1.00 66		6
	MOTA	1406		VAL A		54.771	16.532	39.564	1.00 65		6
15	ATOM	1407	С	VAL A	176	53.495	13.025	38.645	1.00 67		6
	MOTA	1408	0	VAL A		54.399	12.308	38.230	1.00 66		8
	ATOM	1409	N	THR A	A 177	52.213	12.833	38.348	1.00 68		7
	MOTA	1410	CA	THR A	A 177	51.781	11.763	37.463	1.00 69		6
	MOTA	1411	CB	THR A		51.241	10.565	38.259	1.00 69		6
20	MOTA	1412	OG1	THR A		50.218	11.007	39.160	1.00 69		8
	MOTA	1413	CG2	THR A		52.366	9.905	39.045	1.00 69		6
	MOTA	1414	С		A 177		12.276	36.528	1.00 70		6
	MOTA	1415	0		A 177	49.879	13.119	36.917	1.00 72		8
	MOTA	1416	N		A 178	50.692	11.771	35.297	1.00 71		7 6
25	MOTA	1417	CA		A 178	49.706	12.191	34.302	1.00 73		6
	MOTA	1418	CB		A 178	50.392	12.916	33.144			6
	ATOM	1419	CG		A 178	51.681	13.640	33.533	1.00 78		6
	ATOM	1420	CD		A 178	52.059	14.733	32.539	1.00 /3		8
00	ATOM	1421		GLN .		52.078	14,509	31.315 33.061	1.00 78		7
30	MOTA	1422			A 178	52.370	15.924 10.964	33.764	1.00 7		6
	MOTA	1423	С		A 178	49.014	10.944	33.704	1.00 7		8
	MOTA	1424	0		A 178	49.679 47.686	10.043	33.827	1.00 7		7
	ATOM	1425	N		A 179	46.916	9.807	33.337	1.00 7		6
05	MOTA	1426	CA		A 179 A 179	46.327	9.038	34.519	1.00 7		6
35	ATOM	1427	CB		A 179	47.352	8.781	35.644	1.00 7		6
	MOTA	1428	CG CD		A 179	46.703	8.189	36.905	1.00 8		6
	MOTA	1429 1430	CE		A 179	47.635	8.300	38.119	1.00 8		6
	ATOM	1431	NZ		A 179	47.968	9.715	38.443	1.00 8		7
40	MOTA MOTA	1431	C		A 179	45.795	10.316	32.470	1.00 7		6
+0	MOTA	1433	Ö		A 179	44.878	10.939	32.980	1.00 7	3.37	8
	ATOM	1434	Ŋ		A 180	45.845	10.060	31.170	1.00 6	7.55	7
	MOTA	1435	CA		A 180	44.780	10.538	30.294	1.00 6		6
	ATOM	1436	СВ	LYS	A 180	45.171	10.327	28.829	1.00 6		6
45	MOTA	1437	CG		A 180	45.120	8.909	28.344	1.00 6		6
	ATOM	1438	CD	LYS	A 180	43.751	8.573	27.796	1.00 6		6
	ATOM	1439	CE	LYS	A 180	43.404	9.412	26.552	1.00 6		6
	ATOM	1440	NZ		A 180	44.217	9.057	25.339	1.00 6		7
	ATOM	1441	С	LYS	A 180	43.445	9.854	30.586	1.00 6		6
50	ATOM	1442	0	LYS	A 180	43.373	9.021	31.471	1.00 6		8
	ATOM	1443	N		A 181	42.388	10.231	29.871	1.00 6		7
	MOTA	1444	CA		A 181		9.600	30.053	1.00 6		6
	MOTA	1445			A 181		9.514	31.545	1.00 6		6
	MOTA	1446			A 181		10.803	32.291	1.00 6		6 8
55	MOTA	1447			A 181		11.872	31.834	1.00 /		7
	ATOM	1448			A 181		10.706	33.463	1.00 6		
	ATOM	1449			A 181		10.194	29.272 29.437	1.00 6		8
	MOTA	1450			A 181		11.350 9.377	28.420	1.00 6		7
60	MOTA	1451			A 182		9.802	27.615			6
60	MOTA	1452			A 182		8.745	26.553	1.00 6		6
	MOTA	1453	CB	コピス	A 182	37.001	0.740	20.300		<b></b>	_

	WO 01/5	8951				PCT/EP01/01457					
						-96					
	ATOM	1454	OG	SER A 1	82	36.90	9.223	25.626	1.00 70.87	8	
	ATOM	1455	C	SER A 1		36.95		28.541	1.00 67.36	6	
	ATOM	1456	ō	SER A 1		36.91		29.617	1.00 67.61	8	
	MOTA	1457	N	VAL A 1		35.97			1.00 65.82	7	
5	ATOM	1458	CA	VAL A 1		34.79		28.950	1.00 64.66	6	
	ATOM	1459	CB	VAL A 1	L83	35.15			1.00 63.68	· 6	
	MOTA	1460		VAL A 1		36.15			1.00 65.08	6	
	MOTA	1461		VAL A 1		33.90			1.00 61.80	6	
40	ATOM	1462	C ,	VAL A 1		33.63			1.00 64.12 1.00 64.83	6 8	
10	MOTA	1463	0	VAL A		33.82 32.42			1.00 65.00	7	
	ATOM ATOM	1464 1465	N CA	THR A I		31.24			1.00 67.07	6	
	ATOM	1466	CB	THR A		30.30			1.00 64.63	6	
	ATOM	1467		THR A		30.97			1.00 61.46	8	
15	ATOM	1468	CG2			29.03			1.00 67.30	6	
-	ATOM	1469	C	THR A	184	30.49	0 12.596	28.808	1.00 69.96	6	
	MOTA	1470	0	THR A	184	30.41			1.00 71.87	8	
	MOTA	1471	N	TYR A		29.96			1.00 71.00	7	
	MOTA	1472	CA	TYR A		29.23			1.00 72.17	6	
20	ATOM	1473	CB	TYR A		29.84			1.00 72.39	6	
	ATOM	1474	CG	TYR A		31.33			1.00 72.53 1.00 71.50	6 6	
	ATOM	1475		TYR A		32.22 33.60			1.00 71.30	6	
	ATOM ATOM	1476 1477		TYR A		31.85			1.00 73.42	6	
25	ATOM	1478	CE2	TYR A		33.23			1.00 71.16	6	
20	ATOM	1479	CZ	TYR A		34.09			1.00 70.35	6	
	ATOM	1480	OH	TYR A		35.44			1.00 68.69	8	
	ATOM	1481	С	TYR A		27.80		28.780	1.00 73.84	6	
	MOTA	1482	0	TYR A	185	27.55			1.00 73.39	8	
30	MOTA	1483	N	SER A		26.87			1.00 76.31	7	
	ATOM	1484	CA	SER A					1.00 78.23	6	
	ATOM	1485	CB	SER A		24.64			1.00 78.92	6 8	
	ATOM	1486	OG	SER A		25.21			1.00 77.75 1.00 78.29	6	
35	MOTA	1487	C	SER A SER A		25.19 24.34			1.00 78.29	8	
33	MOTA MOTA	1488 1489	O N	CYS A		25.94			1.00 77.81	7	
	ATOM	1490	CA	CYS A		25.83			1.00 78.71	6	
	MOTA	1491	C	CYS A		26.14			1.00 78.06	6	
	ATOM	1492	ō	CYS A		25.51			1.00 78.32	8	
40	MOTA	1493	СВ	CYS A		26.85	8 19.320	28.252	1.00 79.52	6	
,	MOTA	1494	SG	CYS A	187	28.65			1.00 82.56	16	
	MOTA	1495	N	CYS A		27.14			1.00.78.96	7	
	MOTA	1496	CA	CYS A		27.70			1.00 78.72	6	
45	ATOM	1497	C	CYS A		27.81			1.00 78.19	6	
45	MOTA	1498	0	CYS A		28.45			1.00 78.27 1.00 79.96	8 6	
	ATOM	1499	CB	CYS A		29.07 29.11			1.00 79.90	16	
	ATOM ATOM	1500 1501	SG N	CYS A		27.23			1.00 77.44	7	
	ATOM	1501	CD	PRO A		26.57			1.00 77.01	6	
50	ATOM	1502	CA	PRO A		27.12			1.00 76.01	6	
-	ATOM	1504	CB	PRO A		26.75			1.00 76.94	6	
	ATOM	1505	CG	PRO A		25.85			1.00 77.54	6	
	MOTA	1506	С	PRO A		28.35			1.00 75.22	6	
	ATOM ·		0	PRO A		28.30			1.00 76.90	8	
55	MOTA	1508	N	GLU A		29.44			1.00 72.83	7	
	ATOM	1509	CA	GLU A		30.66			1.00 69.68 1.00 72.91	6 6	
	MOTA	1510	CB	GLU A		31.53 30.71			1.00 72.91	6	
	MOTA MOTA	1511 1512	CG CD	GLU A GLU A		30.7			1.00 73.89	6	
60	MOTA	1512		GLU A		30.2			1.00 78.51	8	
	MOTA	1514		GLU A		29.0			1.00 79.55	8	
	<del></del> -				-						

							-97				
	ATOM	1515	c ·	GLU A	. 1	L90	31.492	12.631	23.039	1.00 66.30	6
	ATOM	1516		GLU A				13.278	24.009	1.00 65.23	8
	MOTA	1517		ALA F			32.633	11.941	23.020	1.00 63.17	7
	MOTA	1518		ALA A			33.524	11.891	24.182	1.00 61.94	6
5	ATOM	1519		ALA A			34.102	10.493	24.341	1.00 60.63	6
•	ATOM	1520		ALA A			34.666	12.904	24.055	1.00 61.30	6
	ATOM	1521		ALA A			35.148	13.165	22.950	1.00 62.21	8
	ATOM	1522		TYR A			35.105	13.468	25.179	1.00 58.30	7
	ATOM	1523	CA	TYR A	A :	192	36.188	14.438	25.159	1.00 56.19	6
10	ATOM	1524		TYR A	A :	192	35 <i>.</i> 695	15.807	25.633	1.00 55.84	6
	MOTA		CG	TYR A	A :	192	34.779	16.487	24.649	1.00 56.15	6
	MOTA	1526	CD1	TYR A	A :	192	33.409	16.226	24.642	1.00 56.04	6
	MOTA	1527	CE1	TYR 2	Α :	192	32.571	16.794	23.683	1.00 57.88	6
	ATOM	1528	CD2	TYR I	Α :	192	35.291	17.341	23.675	1.00 56.39	6
15	MOTA	1529	CE2	TYR 3	Α :	192	34.467	17.915	22.715	1.00 57.19	6
	ATOM	1530	CZ	TYR 2	Α :	192	33.108	17.637	22.722	1.00 58.29	6
	MOTA	1531	OH ·	TYR	Α.	192	32.295	18.200	21.769	1.00 58.06	8
	MOTA	1532	С	TYR .	Α.	192	37.389	14.013	25.984	1.00 56.62	6
	MOTA	1533	0	TYR .			37.375	14.090	27.217	1.00 57.67	8
20	MOTA	1534	N	GLU .			38.436	13.571	25.291	1.00 57.15	7
	MOTA	1535	CA	GLU .			39.676	13.124	25.935	1.00 58.07	6
	MOTA	1536	CB	GLU			40.651	12.523	24.901	1.00 56.63	6
	MOTA	1537	CG	GLU .			40.143	11.269	24.209	1.00 55.92	6
	MOTA	1538	CD	GLU			41.171	10.636	23.307	1.00 56.05	6
25	MOTA	1539		GLU			42.339	10.509	23.743	1.00 56.33	8
	MOTA	1540		GLU			40.808	10.250	22.171	1.00 57.19	8
	MOTA	1541	С	GLU			40.363	14.278	26.655	1.00 58.09	6
	MOTA	1542	0	GLU			40.221	15.440	26.261	1.00 59.15	8
	MOTA	1543	N	ASP			41.098	13.948	27.712	1.00 57.73	7 6
30	ATOM	1544	CA	ASP			41.816	14.941	28.486	1.00 56.31 1.00 57.85	6
	MOTA	1545	CB	ASP			40.856	15.738	29.386 30.578	1.00 57.85	6
	MOTA	1546	CG OD1	ASP			40.339	14.930 14.610	30.578	1.00 55.87	8
	MOTA	1547		ASP			39.120 41.154	14.628	31.494	1.00 58.60	8
25	MOTA	1548		ASP			42.881	14.026	29.333	1.00 55.87	6
35	MOTA	1549 1550	C	ASP ASP			42.746	13.121	29.714	1.00 56.72	8
	ATOM	1551	N O	VAL			43.948	15.014	29.611	1.00 55.00	7
	MOTA MOTA	1551	CA	VAL			45.039	14.520	30.431	1.00 55.58	6
	ATOM	1553	CB	VAL			46.397	14.961	29.876	1.00 54.15	6
40	MOTA	1554		VAL			47.508	14.610	30.860	1.00 52.00	6
40	ATOM	1555		VAL			46.643	14.292	28.544	1.00 53.83	6
	ATOM	1556	C	VAL			44.900	15.082	31.832	1.00 57.46	6
	ATOM	1557	ō	VAL			44.809	16.294	32.011	1.00 57.93	8
	ATOM	1558	N	GLU			44.886	14.206	32.828	1.00 58.46	7
45	ATOM	1559	CA	GLU			44.767	14.654	34.204	1.00 58.24	6
	ATOM	1560	CB	GLU	Α	196	43.805	13,758	34.966	1.00 59.77	6
	MOTA	1561	CG	GLU	Α	196	43.556	14.199	36.385	1.00 63.27	6
	MOTA	1562	CD	GLU	Α	196	42.624	13.256	37.114	1.00 64.52	6
	MOTA	1563	QE1	GLU	Α	196	41.485	13.063	36.646	1.00 63.73	8
50	MOTA	1564	OE2	GLU	A	196	43.035	12.705	38.155	1.00 68.58	8
	MOTA	1565	С	GLU	A	196	46.142	14.590	34.828	1.00 57.57	6
	MOTA	1566	0	GLU			46.775	13.538	34.841	1.00 59.03	8
	MOTA	1567	N	VAL			46.618	15.723	35.322	1.00 55.78	7
	MOTA	1568	CA	VAL			47.929	15.766	35.943	1.00 55.65	6
55	MOTA	1569		VAL			48.781	16.937	35.386	1.00 55.24	6
	MOTA	1570		VAL			50.142	16.962	36.050	1.00 51.21	6
	MOTA	1571		VAL			48.929	16.800	33.877	1.00 53.65 1.00 57.58	6
	ATOM	1572				197		15.955	37.431 37.850	1.00 57.58	6 8
60	MOTA	1573				197	46.963 48 355	16.843 15.102	38.231	1.00 57.88	7
60	MOTA	1574				198	48.355 48.229	15.102	39.677	1.00 57.91	6
	MOTA	1575	CA	SUL	v	198	40.223		55.577	57.51	•

					-98				
	MOTA	1576	СВ	SER A 198	47.951	13.822	40.275	1.00 56.54	6
	MOTA	1577		SER A 198	46.654	13.401	39.908	1.00 61.46	8
	ATOM	1578		SER A 198	49.501	15.765	40.257	1.00 58.27	6
	MOTA	1579		SER A 198	50.585	15.202	40.089	1.00 58.63	8
5	ATOM	1580	N	LEU A 199	49.366	16.901	40.929	1.00 58.53	7
_	ATOM	1581	CA	LEU A 199	50.521	17.538	41.531	1.00 60.77	6
	MOTA	1582	CB	LEU A 199	50.519	19.046	41.274	1.00 60.73	6
	MOTA	1583	CG	LEU A 199	51.591	19.833	42.032	1.00 59.19	6
	MOTA	1584		LEU A 199	52.982	19.400	41.599	1.00 57.61	6
10	MOTA	1585	CD2	LEU A 199	51.390	21.311	41.776	1.00 60.66	6
	MOTA	1586	С	LEU A 199	50.524	17.293	43.022	1.00 61.78 1.00 62.31	6 8
	MOTA	1587	0	LEU A 199	49.739	17.895	43.765	1.00 62.31	7
	ATOM	1588	N	ASN A 200	51.397	16.389	43.457 44.866	1.00 58.00	6
	MOTA	1589	CA	ASN A 200	51.519	16.092	45.088	1.00 58.00	6
15	MOTA	1590	CB	ASN A 200	51.763 51.926	14.607 14.267	46.553	1.00 61.99	6
	ATOM	1591	CG	ASN A 200	51.158	14.735	47.391	1.00 63.14	8
	MOTA	1592		ASN A 200 ASN A 200	52.928	13.447	46.871	1.00 63.54	7
	ATOM	1593		ASN A 200	52.708	16.906	45.345	1.00 56.52	6
20	MOTA	1594	C O	ASN A 200	53.859	16.664	44.957	1.00 55.31	8
20	MOTA ATOM	1595 1596	N	PHE A 201	52.406	17.901	46.166	1.00 55.49	7
	MOTA	1597	CA	PHE A 201	53.416	18.790	46.707	1.00 54.84	6
		1598	CB	PHE A 201	53.450	20.082	45.908	1.00 50.77	6
	MOTA	1599	CG	PHE A 201	52.237	20.940	46.112	1.00 47.21	6
25	MOTA	1600		PHE A 201	52.337	22.161	46.765	1.00 46.20	6
	MOTA	1601		PHE A 201	50.985	20.513	45.678	1.00 46.31	6
	MOTA	1602		PHE A 201	51.205	22.942	46.984	1.00 45.24	6
	MOTA	1603		PHE A 201	49.849	21.291	45.896	1.00 43.16	6
	ATOM	1604	CZ	PHE A 201	49.962	22.504	46.549		6
30	MOTA	1605	С	PHE A 201	53.035	19.112	48.142	1.00 56.47	6
	MOTA	1606	0	PHE A 201	51.956	18.748	48.610	1.00 54.75	8
	MOTA	1607	N	ARG A 202	53.927	19.811	48.829	1.00 58.72	7
	MOTA	1608	CA	ARG A 202	53.693	20.207	50.207	1.00 61.75	6
	ATOM	1609	CB	ARG A 202	54.052	19.063	51.136	1.00 63.76 1.00 65.86	6 6
35	MOTA	1610	CG	ARG A 202	55.544	18.822	51.130	1.00 68.52	6
	ATOM	1611	CD	ARG A 202	55.938	17.640	51.962 51.916	1.00 69.87	7
	MOTA	1612	NE	ARG A 202	57.383	17.466 16.409	52.405	1.00 70.56	6
	MOTA	1613	CZ	ARG A 202	58.013 57.308	15.433	52.977	1.00 70.30	7
40	MOTA	1614		ARG A 202 ARG A 202	59.340	16.332	52.315	1.00 70.56	7
40	MOTA	1615	NH2	ARG A 202	54.579	21.406	50.556	1.00 62.74	6
	MOTA	1616 1617		ARG A 202 ARG A 202	55.588	21.675	49.890	1.00 62.41	8
	MOTA	1618	. N	LYS A 203	54.200	22.121		1.00 63.53	7
	ATOM ATOM	1619		LYS A 203	54.983	23.256	52.044	1.00 64.89	6
45	MOTA	1620		LYS A 203	54.271	23.993	53.169	1.00 65.59	6
40	ATOM	1621		LYS A 203	55.067	25.149	53.740	1.00 66.14	6
	ATOM	1622		LYS A 203	54.348	25.777	54.911	1.00 65.85	6
	ATOM	1623		LYS A 203	55.145	26.939	55.473	1.00 67.46	6
	ATOM	1624		LYS A 203	55.259	28.073	54.500	1.00 68.09	7
50	MOTA	1625		LYS A 203	56.264	22.665	52.563	1.00 65.93	6
	MOTA	1626	0	LYS A 203	56.250	21.585	53.157	1.00 66.11	8
	MOTA	1627	N	LYS A 204	57.372	23.351	52.313	1.00 69.05	7
	MOTA	1628		LYS A 204	58.659	22.863	52.767	1.00 71.58	6
·	ATOM	1629		LYS A 204	59.758	23.834	52.358	1.00 69.66	6
55	ATOM	1630		LYS A 204	59.862	23.906	50.839	1.00 69.91 1.00 71.48	6 6
	ATOM	1631		LYS A 204	61.113	24.609	50.336		6
	MOTA	1632		LYS A 204	61.195	24.491	48.809 48.189		7
	MOTA	1633		LYS A 204	62.324 59.544				6
60	MOTA	1634		LYS A 204 LYS A 204	58.544 57.769				8
60	MOTA	1635		GLY A 205	59.262		54.850		7
	MOTA	1636	<i>N</i>	GDI A 203	202,202	22.702	52.550		•

	WO 01/5	8951				PCT/EP01/01457				457	
							-99				
	ATOM	1637	CA	GLY	A 205	;	59.215	21.592	56.296	1.00 75.55	6
	ATOM ·	1638	С	GLY	A 205	i	60.125	22.564	57.029	1.00 76.09	6
	MOTA	1639	OT1	GLY	A 205	i	60.824	23.350	56.348	1.00 77.07	8
	MOTA	1640	OT2	GLY	A 205	j	60.151	22.545	58.278	1.00 75.36	8
5	MOTA	1641	CB	PHE	в 1		33.107	19.922	1.832	1.00 57.02	6
	ATOM	1642	CG	PHE		-	32.174	20.672	0.888	1.00 58.55	· 6
	ATOM	1643		PHE		-	32.670	21.495	-0.120	1.00 59.39	6
	ATOM	1644		PHE			30.784	20.612	1.079	1.00 58.84	6
	MOTA	1645		PHE			31.795	22.248	-0.919	1.00 59.92	6
10	ATOM	1646		PHE			29.905	21.357	0.292	1.00 56.97	6
	MOTA	1647	CZ	PHE			30.410	22.176	-0.707	1.00 58.52	6
	ATOM	1648	C	PHE			35.200	18.747	2.262	1.00 56.22	6
	MOTA	1649	0	PHE			34.732	18.314	3.311	1.00 58.27	8 7
4 =	MOTA	1650		PHE			33.748	17.916	0.462	1.00 54.28 1.00 55.90	6
15	MOTA	1651	CA	PHE			34.250	19.143 18.877	1.152 2.083	1.00 55.90	7
	MOTA	1652 1653	N	ASP ASP			36.512 37.383	18.526	3.204	1.00 55.33	6
	MOTA MOTA	1654	CA CB	ASP			38.876	18.485	2.792	1.00 59.88	6
	ATOM	1655	CG	ASP			39.364	19.782	2.139	1.00 65.04	6
20	ATOM	1656		ASP		2	40.076	19.729	1.091	1.00 67.12	8
	ATOM	1657		ASP			39.042	20.860	2.684	1.00 68.18	8
	ATOM	1658	C	ASP			37.096	19.582	4.280	1.00 55.70	6
	ATOM	1659	Ö	ASP		2	36.331	20.507	4.047	1.00 54.61	8
	ATOM	1660	N	ARG			37.682	19.443	5.458	1.00 55.52	7
25	ATOM	1661	CA	ARG		3	37.441	20.380	6.556	1.00 53.72	6
	ATOM	1662	СВ	ARG	в 3	3	38.114	19.838	7.806	1.00 56.23	6
	ATOM	1663	CG	ARG	в :	3	37.541	20.323	9.094	1.00 55.76	6
	MOTA	1664	CD	ARG		3	37.772	19.269	10.139	1.00 55.83	6
	ATOM	1665	NE	ARG		3	36.531	18.930	10.818	1.00 56.35	7
30	ATOM	1666	CZ	ARG		3	36.233	17.708	11.220	1.00 56.91	6
	ATOM	1667		ARG		3	37.095	16.729	10.994	1.00 56.22	7
	ATOM	1668		ARG		3	35.090	17.468	11.849	1.00 57.84	7
	ATOM	1669	C	ARG		3	37.909	21.822	6.295	1.00 53.67	6
0=	MOTA	1670	0	ARG		3	37.395	22.772	6.888	1.00 53.80	8 7
35	MOTA	1671	N	ALA		1 1	38.896	21.969 23.255	5.420 5.025	1.00 52.29 1.00 50.06	6
	MOTA	1672 1673	CA CB	ALA ALA		± 1	39.443 40.743	23.235	4.275	1.00 48.42	6
	MOTA MOTA	1674	СВ	ALA		± <u>1</u>	38.442	23.030	4.131	1.00 49.06	6
	ATOM	1675	0	ALA		<del>-</del> 4	38.225	25.179	4.270	1.00 47.12	8
40	ATOM	1676	N	ASP		5	37.837	23.233	3.211	1.00 49.07	7
-10	ATOM	1677	CA	ASP		5	36.869	23.801	2.288	1.00 51.75	6
	MOTA	1678	СВ	ASP		5	36.345	22.748	1.299	1.00 55.02	6
	ATOM	1679	CG	ASP	в :	5	37.454	22.084	0.491	1.00 60.18	6
	MOTA	1680	OD1	ASP		5	38.347	22.794	-0.039	1.00 63.04	8
45	MOTA	1681		ASP		5	37.430	20.839	0.374	1.00 61.10	8
	MOTA	1682	С	ASP	В	5	35.699	24.381	3.051	1.00 51.17	6
	MOTA	1683	0	ASP	B .	5	35.179	25.428	2.670	1.00 51.32	8
	MOTA	1684	N	ILE	В	6	35.292	23.713	4.130	1.00 49.73	7
	MOTA	1685	CA	ILE		6	34.164	24.178	4.926	1.00 50.09	6
50	ATOM	1686	CB	ILE		6	33.723	23.128	5.950	1.00 51.11	6
	MOTA	1687		ILE		6	32.472	23.610	6.678	1.00 48.60	6
	MOTA	1688		ILE		6	33.434	21.809	5.232	1.00 53.13	6
	ATOM	1689		ILE		6	32.881	20.712	6.121	1.00 55.06 1.00 49.98	6
55	ATOM	1690	C	ILE		6	34.448	25.480	5.653	1.00 49.98	6 8
55	ATOM	1691	0	LEU		6 7	33.700 35.524	26.450 25.504	5.518 6.426	1.00 51.60	8 7
	MOTA	1692 1693	N CA	TEU		, 7	35.524	26.705	7.160	1.00 49.48	6
	ATOM ATOM	1694	CB	LEU		, 7	37.157	26.424	7.100	1.00 45.60	6
	ATOM	1695	CG	LEU		, 7	36.916	25.427	9.126	1.00 45.98	6
60	MOTA	1696		LEU		7	38.221	24.935	9.696	1.00 46.59	6
	ATOM	1697		LEU		7	36.081	26.086	10.191	1.00 44.50	6
		'									

	WO 01/5	8951									PCT/EP01/01	457
								-100				
	ATOM	1698	c :	LEU E	2	7		36.167	27.850	6.195	1.00 47.43	6
	ATOM	1699	_	LEU E		7		35.797	28.986	6.447	1.00 46.94	8
	ATOM	1700		TYR I		8		36.799	27.529	5.080	1.00 49.45	7
	ATOM	1701		TYR I		8		37.105	28.507	4.051	1.00 52.16	6
5	ATOM	1702		TYR E		8		37.800	27.821	2.877	1.00 54.75	6
J	ATOM	1703		TYR I		8		38.090	28.758	1.737	1.00 56.10	6
	ATOM	1704		TYR I		8		39.088	29.720	1.839	1.00 56.48	6
	ATOM	1705	CE1	TYR I	В	8		39.344	30.605	0.794	1.00 57.35	6
	ATOM	1706	CD2	TYR I	В	8		37.348	28.701	0.564	1.00 57.26	6
10	ATOM	1707	CE2	TYR I	В	8		37.592	29.581	-0.484	1.00 57.99	6
	MOTA	1708	CZ	TYR I	В	8		38.590	30.528	-0.364	1.00 57.33	6
	MOTA	1709	OH	TYR I	В	8		38.819	31.385	-1.408	1.00 58.94	8
	MOTA	1710		TYR :		8		35.858	29.234	3.537	1.00 52.55	6
	MOTA	1711		TYR 1		8		35.867	30.460	3.387	1.00 52.22	8 7
15	MOTA	1712		ASN		9		34.796	28.482	3.249	1.00 52.51 1.00 54.09	6
	MOTA	1713		ASN :		9		33.566	29.086 28.021	2.752 2.376	1.00 56.72	6
	ATOM	1714	CB	ASN :		9		32.539 32.963	27.203	1.163	1.00 50.72	6
	MOTA	1715	CG	ASN		9		33.966	27.509	0.512	1.00 61.72	8
20	MOTA	1716		ASN ASN		9 9		32.198	26.159	0.852	1.00 61.67	7
20	MOTA	1717 1718	C	ASN		9		32.980	30.007	3.794	1.00 54.24	6
	ATOM ATOM	1719	0	ASN		. 9		32.680	31.160	3.506	1.00 54.66	8
	MOTA	1720	Ŋ	ILE		10		32.829	29.503	5.013	1.00 54.21	7
	ATOM	1721	CA	ILE		10	٠	32.282	30.310	6.104	1.00 53.77	6
25	ATOM	1722	CB	ILE		10		32.303	29.543	7.429	1.00 52.00	6
	ATOM	1723	CG2	ILE		10		31.860	30.451	8.552	1.00 50.79	6
	ATOM	1724	CG1	ILE		10		31.389	28.323	7.339	1.00 50.43	6
	ATOM	1725	CD1	ILE	В	10		31.531	27.371	8.498	1.00 47.56	6
	MOTA	1726	С	ILE	В	10		33.085	31.592	6.284	1.00 55.12	6
30	ATOM	1727	0	ILE	В	10		32.531	32.663	6.458	1.00 56.17	8
	MOTA	1728	N	ARG		11		34.400	31.464	6.243	1.00 56.91	7 6
	MOTA	1729	CA	ARG		11		35.297	32.595	6.386	1.00 58.48 1.00 63.85	6
	MOTA	1730	CB	ARG		11		36.739	32.110	6.243 6.434	1.00 68.86	6
05	MOTA	1731	CG	ARG		11		37.799 37.917	33.170 33.493	7.917	1.00 00.00	6
35	ATOM	1732	CD	ARG		11 11		39.211	34.078	8.264	1.00 85.52	7
	ATOM ATOM	1733 1734	NE CZ	ARG ARG		11		40.384	33.635	7.807	1.00 88.55	6
	ATOM	1735		ARG		11		40.424	32.589	6.970	1.00 90.95	7
	ATOM	1736		ARG		11		41.518	34.239	8.178	1.00 87.63	7
40	ATOM	1737	C	ARG		11		35.030	33.639	5.306	1.00 58.49	6
40	ATOM	1738	Ö	ARG		11		34.905	34.825	5.584	1.00 57.34	8
	ATOM	1739	N	GLN		12		34.933	33.175	4.066	1.00 58.50	7
	ATOM	1740	CA	GLN		12		34.748	34.055	2.927	1.00 57.77	6
	ATOM	1741	СВ	GLN	В	12		35.147	33.329	1.653	1.00 58.35	6
45	MOTA	1742	CG	GLN	В	12		36.124	34.100	0.814	1.00 62.22	6
	ATOM	1743	CD	GLN		12		37.514	33.973	1.351	1.00 64.08	6
	MOTA	1744		GLN		12		38.011	32.862	1.501	1.00 68.35	8
	MOTA	1745		GLN		12		38.156	35.098	1.653	1.00 63.78 1.00 57.86	7 6
	MOTA	1746	C	GLN		12		33.366	34.633	2.720 2.059	1.00 57.86	8
50	ATOM	1747	0	GLN		12		33.219	35.657 33.994	3.266	1.00 57.21	7
	ATOM	1748	N	THR		13 13		32.345 30.987	34.479	3.054	1.00 56.88	6
	MOTA	1749	CA	THR THR		13		30.101	33.373	2.468	1.00 54.90	6
•	MOTA	1750 1751	CB OG1			13		30.100	32.247	3.350	1.00 55.07	8
55	MOTA MOTA	1751	CG2			13		30.612	32.946	1.104	1.00 56.83	6
55	ATOM	1752	C	THR		13		30.295	35.009	4.298	1.00 58.52	6
	ATOM	1754	Ö	THR		13		29.275	35.698	4.206	1.00 57.64	8
	ATOM	1755		SER		14		30.848		5.462	1.00 60.24	7
	MOTA	1756		SER		14		30.247	35.117	6.715	1.00 60.31	6
60	ATOM	1757		SER		14		30.884		7.878	1.00 60.50	6
	MOTA	1758	OG	SER	В	14		30.086	34.485	9.034	1.00 63.18	8

	WO 01/5	8951								PCT/EP01/01	457
							-101		•		
	ATOM	1759	С	SER	В	14	30.343	36.619	6.949	1.00 59.80	6
	MOTA	1760	ō	SER		14	31.247	37.293	6.443	1.00 60.23	8
	MOTA	1761	N	ARG	В	15	29.382	37.134	7.710	1.00 58.15	7
	MOTA	1762	CA	ARG	В	15	29.322	38.549	8.040	1.00 55.80	6
5	ATOM	1763	CB	ARG		15	28.271	39.239	7.183	1.00 56.87	6
	ATOM	1764	CG	ARG		15	28.540	39.145	5.684	1.00 60.72	
	MOTA	1765	CD	ARG		15	27.721	40.179	4.945	1.00 63.19	6
	MOTA	1766	NE	ARG		15	28.008	41.515	5.475	1.00 67.21	7
40	ATOM	1767	CZ	ARG		15	27.307	42.616	5.196	1.00 67.82	6
10	MOTA	1768		ARG		15	26.259	42.549	4.384	1.00 69.12	7 7
	ATOM	1769		ARG		15	27.660	43.789 38.655	5.722 9.511	1.00 66.84 1.00 54.09	6
	ATOM ATOM	1770 1771	C	ARG ARG		15 15	28.962 27.795	38.651	9.880	1.00 55.59	8
	ATOM	1772	N O	PRO		16	29.979	38.747	10.377	1.00 51.42	7
15	ATOM	1773	CD	PRO		16	31.405	38.751	10.015	1.00 48.17	6
. •	ATOM	1774	CA	PRO		16	29.817	38.846	11.828	1.00 48.94	6
	ATOM	1775	CB	PRO		16	31.256	38.950	12.328	1.00 48.44	6
	ATOM	1776	CG	PRO	В	16	32.038	38.262	11.284	1.00 48.62	6
	ATOM	1777	С	PRO	В	16	28.974	40.014	12.300	1.00 48.35	6
20	MOTA	1778	0	PRO	В	16	28.475	40.006	13.420	1.00 49.87	8
	MOTA	1779	N	ASP		17	28.825	41.026	11.456	1.00 49.55	. 7
	ATOM	1780	CA	ASP		17	28.048	42.201	11.830	1.00 51.87	6
	ATOM	1781	CB	ASP		17	28.638	43.469	11.204	1.00 55.73	6
05	ATOM	1782	CG	ASP		17	29.956	43.896	11.856	1.00 59.93	6
25	ATOM	1783		ASP		17	30.158	43.598	13.062	1.00 60.57 1.00 61.01	8 8
	ATOM	1784	C OD2	ASP		17 17	30.781 26.581	44.548 42.120	11.163 11.458	1.00 51.65	6
	MOTA MOTA	1785 1786	0	ASP ASP		17	25.837	43.066	11.438	1.00 51.05	8
	MOTA	1787	N	VAL		18	26.156	40.990	10.906	1.00 53.24	7
30	ATOM	1788	CA	VAL		18	24,772	40.848	10.495	1.00 53.38	6
00	ATOM	1789	CB	VAL		18	24.679	40.682	8.978	1.00 52.53	6
	ATOM	1790		VAL		18	23.238	40.628	8.551	1.00 53.33	⁻ 6
	ATOM	1791	CG2	VAL	В	18	25.385	41.833	8.299	1.00 52.08	6
	ATOM	1792	С	VAL	В	18	24.026	39.701	11.157	1.00 54.80	6
35	MOTA	1793	0	VAL		18	24.359	38.527	10.980	1.00 57.05	8
	MOTA	1794	N	ILE		19	22.999	40.062	11.913	1.00 55.38	7
	ATOM	1795	CA	ILE		19	22.150	39.105	12.615	1.00 54.84	6
	ATOM	1796	CB	ILE		19	21.128	39.899	13.493	1.00 53.97	6
40	ATOM	1797		ILE		19	20.177	40.699	12.612	1.00 52.99	6
40	MOTA	1798		ILE		19	20.354	38.963	14.414	1.00 54.58	6
	MOTA	1799		ILE		19	19.598 21.450	39.696 38.192	11.586	1.00 51.38 1.00 55.77	6 6
	ATOM ATOM	1800 1801	С С	ILE		19 19	20.879	38.678	10.605	1.00 56.23	8
	ATOM	1801	Ŋ	PRO		20	21.508	36.857	11.787	1.00 57.54	7
45	MOTA	1803	CD	PRO		20	22.223	36.204	12.888	1.00 57.31	6
	ATOM	1804	CA	PRO		20	20.900	35.841	10.900	1.00 59.26	6
	ATOM	1805	СВ	PRO		20	21.478	34.521	11.417	1.00 57.46	6
	ATOM	1806	CG	PRO	В	20	22.657	34.935	12.235	1.00 58.77	6
	MOTA	1807	С	PRO	В	20	19.366	35.836	10.940	1.00 62.02	6
50	ATOM	1808	0	PRO	В	20	18.732	34.806	11.185	1.00 61.74	8
	MOTA	1809	N	THR		21	18.781	36.997	10.679	1.00 65.81	7
	MOTA	1810	CA	THR		21	17.337	37.160	10.705	1.00 69.72	6
	ATOM	1811	CB	THR		21	16.974	38.658	10.971	1.00 67.96	6
EF	MOTA	1812		THR		21	16.710	38.837	12.367	1.00 69.51	8
55	MOTA	1813	CG2			21	15.765	39.087	10.178	1.00 68.09 1.00 73.11	6 6
	ATOM	1814	C	THR THR		21 21	16.606 17.000	36.658 36.942	9.455 8.315	1.00 73.11	8
	ATOM ATOM	1815 1816	O N	GLN		22	15.532	35.907	9.694	1.00 71.83	7
	ATOM	1817	CA	GLN		22	14:684	35.370	8.629	1.00 77.43	6
60	ATOM	1818	CB	GLN		22	14.492	33.871	8.842	1.00 81.72	,6
- <b>-</b>	ATOM	1819	CG	GLN		22	15.793	33.097	8.917	1.00 83.16	6

	WO 01/58	8951					PCT/EP01/01457					
							-102					
	MOTA	1820	CD	GLN	B	22	15.654	31.832	9.753	1.00 8	35.69	6
	ATOM	1821		GLN		22	15.421	31.901	10.976	1.00 8		8
	ATOM	1822		GLN		22	15.787	30.665	9.103	1.00 8	35.85	7
	ATOM	1823		GLN		22	13.326	36.091	8.717	1.00 8	31.72	6
5	ATOM	1824	0	GLN	В	22	12.526	35.837	9.632	1.00 8		8
	ATOM	1825	N	ARG	В	23	13.075	36.990	7.765	1.00 8		7
	MOTA	1826	CA	ARG		23	11.829	37.769	7.744	1.00		6
	ATOM	1827	СB	ARG		23	10.599	36.840	7.695	1.00		6
40	MOTA	1828	CG	ARG		23	10.348	36.215	6.314	1.00		6 6
10	MOTA	1829	CD	ARG		23	10.796 10.694	34.734	6.215 4.833	1.00		7
	ATOM	1830	NE	ARG		23 23	9.590	34.242 34.302	4.053	1.00		6
	ATOM ATOM	1831 1832	CZ	ARG ARG		23	8.452	34.832	4.534	1.00		7
	ATOM	1833		ARG		23	9.627	33.855	2.811	1.00		7
15	ATOM	1834	C	ARG		23	11.754	38.657	8.987	1.00		6
	ATOM	1835	Ö	ARG		23	12.776	39.137	9.476	1.00		8
	ATOM	1836	N	ASP		24	10.548	38.879	9.497	1.00	86.08	7
	ATOM	1837	CA	ASP		24	10.393	39.703	10.693	1.00	85.72	6
	MOTA	1838	СВ	ASP	В	24	8.975	40.301	10.799	1.00		6
20	MOTA	1839	CG	ASP	В	24	8.226	40.339	9.453	1.00		6
	MOTA	1840		ASP		24	8.743	40.965	8.486	1.00		8
	MOTA	1841		ASP		24	7.113	39.746	9.376	1.00		8
	ATOM	1842	С	ASP		24	10.622	38,798	11.891	1.00		6
0-	ATOM	1843	0	ASP		24	10.445	39.218	13.045	1.00		8
25	ATOM	1844	N	ARG		25	10.994	37.549	11.613	1.00 1.00		7 6
	MOTA	1845	CA	ARG		25	11.237	36.584 35.159	12.677 12.128	1.00		6
	MOTA	1846	CB	ARG ARG		25 25	11.318 10.001	34.541	11.696	1.00		6
	ATOM ATOM	1847 1848	CG CD	ARG		25 25	10.001	33.024	11.485	1.00		6
30	ATOM	1849	NE	ARG		25	8.908	32.371	11.140	1.00		7
00	MOTA	1850	CZ	ARG		25	8.747	31.053	11.005	1.00		6
	MOTA	1851		ARG		25	9.785	30.235	11.186	1.00		7
	ATOM	1852		ARG		25	7.538	30.549	10.709	1.00		7
	MOTA	1853	С	ARG		25	12.527	36.876	13.426	1.00	75.18	6
35	MOTA	1854	0	ARG	В	25	13.573	37.105	12.813	1.00		8
	MOTA	1855	N	PRO	В	26	12.463	36.879	14.767	1.00		7
	MOTA	1856	CD	PRO		26	11.233	36.885	15.569	1.00		6
	MOTA	1857	CA	PRO		26	13.629	37.134	15.617		68.20	6
40	MOTA	1858	CB	PRO		26	13.020	37.298	17.007		68.04	6 6
40	ATOM	1859	CG	PRO		26	11.627	37.763 35.917	16.720 15.572	-	68.94 65.66	6
	MOTA	1860	C	PRO		26	14.543 14.114	34.832	15.183	1.00		8
	MOTA MOTA	1861 1862	N	PRO VAL		26 27	15.801	36.093	15.165		62.13	7
	MOTA	1863	CA	VAL		27	16.716	34.969	15.990		58.35	6
45	ATOM	1864	CB	VAL		27	18.185	35.416	15.851		57.74	6
	ATOM	1865		VAL		27	19.127	34.308	16.328	1.00	54.93	6
	ATOM	1866		VAL		27	18.479	35.737	14.393	1.00	54.94	6
	ATOM	1867	C	VAL		27	16.491	34.348	17.349		56.29	6
	MOTA	1868	0	VAL	В	27	16.517	35.043	18.360		56.31	8
50	MOTA	1869	N	ALA		28	16.243	33.045	17.379		54.44	7
	ATOM	1870	CA	ALA			16.008	32.384	18.645		52.98	6
	MOTA	1871	CB	ALA		28	15.095	31.209	18.461		52.15	6
	MOTA	1872	C	ALA		28	17.318	31.938	19.262		52.73	6
ĒE	ATOM	1873	0	ALA		28	17.959	31.004	18.782 20.334		51.86 51.10	8 7
55	MOTA	1874	N	VAL		29	17.696 18.911	32.632 32.353	20.334		49.08	6
	ATOM	1875 1876	CA CB	VAL VAL		29 29	19.741	33.642	21.324		49.72	6
	ATOM ATOM	1877		VAL.		29	20.986	33.323	22.140		46.43	6
	ATOM	1878		VAL		29	20.117	34.272	19.996		49.12	6
60	ATOM	1879	C	VAL		29	18.553	31.762	22.428	1.00	48.65	6
-	ATOM	1880	0	VAL		29	17.731	32.301	23.161	1.00	48.71	8

PCT/EP01/01457

	W O 01/3	10231								rci/Erui/u.	1437
							-103				
			_		2.0			30.638	22.746	1.00 50.09	7
	MOTA	1881	N	SER B	30		19.169	29.997	24.018	1.00 53.68	6
	MOTA	1882		SER B	30		18.925		23.817	1.00 53.36	6
	MOTA	1883	CB	SER B	30		18.587	28.521	23.817	1.00 57.88	8
	MOTA	1884	OG	SER B	30		19.653	27.845	24.823	1.00 56.00	6
5	MOTA	1885	С	SER B	30		20.201	30.150		1.00 57.56	8
	MOTA	1886	0	SER B	30		21.297	29.933	24.306	1.00 57.69	7
	ATOM	1887	N	VAL B	31		20.049	30.542	26.084	1.00 57.05	6
	ATOM	1888	CA	VAL B	31		21.175	30.752	26.980	1.00 57.15	6
	MOTA	1889	CB	VAL B	31		21.227	32.198	27.460	1.00 57.32	6
10	MOTA	1890		VAL B	31		22.536	32.449	28.185	1.00 56.64	6
	MOTA	1891	CG2	VAL B	31		21.044	33.147	26.288		6
	MOTA	1892	С	VAL B	31		21.016	29.878	28.204	1.00 57.98 1.00 59.53	8
	MOTA	1893	0	VAL B	31		19.938	29.815	28.787		
•	MOTA	1894	N	SER B	32		22.101	29.232	28.611	1.00 58.26	7
15	MOTA	1895	CA	SER B	32		22.069	28.356	29.765	1.00 58.30	6
	MOTA	1896	CB	SER B	32		21.806	26.914	29.298	1.00 60.26	6
	MOTA	1897	OG	SER B	32		21.881	25.975	30.361	1.00 61.39	8
	ATOM	1898	С	SER B	32		23.374	28.414	30.530	1.00 58.22	6
	MOTA	1899	0	SER B	32		24.402	27.983	30.024	1.00 62.28	8 7
20	MOTA	1900	N	LEU B	33 ·		23.340	28.937	31.753	1.00 56.90	
	MOTA	1901	CA	LEU B	33		24.548	29.002	32.572	1.00 56.09	6
	MOTA	1902	CB	LEU B	33		24.489	30.183	33.541	1.00 54.84	6
	MOTA	1903	CG	LEU B	33		24.257	31.555	32.914	1.00 55.33	. 6
	ATOM	1904	CD1	LEU B	33		24.483	32.647	33.962	1.00 53.97	6
25	ATOM	1905	CD2	LEU B	33		25.201	31,731	31.737	1.00 56.27	6
	ATOM	1906	C	LEU B	33		24.725	27.728	33.379	1.00 55.50	6
	ATOM	1907	0	LEU B	33		23.770	27.220	33.950	1.00 56.54	8
	MOTA	1908	N	LYS B	34		25.948	27.215	33.413	1.00 55.65	7
	ATOM	1909	CA	LYS E	34		26.270	26.018	34.183	1.00 56.27	6
30	MOTA	1910	CB	LYS E	34		26.815	24.905	33.279	1.00 60.64	6
	MOTA	1911	CG	LYS E	34		25.908	24.528	32.102	1.00 66.07	6
	ATOM	1912	CD	LYS E	34		24.552	23.965	32.566	1.00 72.18	6
	MOTA	1913	CE	LYS F	3 34		23.611	23.670	31.373	1.00 74.46	6
	ATOM	1914	NZ	LYS E	3 34		22.303	23,068	31.799	1.00.74.04	7
35	MOTA	1915	С	LYS E	3 3 4		27.365	26.493	35.108	1.00 54.54	6
	MOTA	1916	0	LYS I			28.463	26.811	34.655	1.00 55.93	8 7
	MOTA	1917	N	PHE			27.079	26.564	36.401	1.00 52.21	6
	MOTA	1918	CA	PHE E			28.086	27.045	37.336	1.00 49.54	
	MOTA	1919	СВ	PHE F			27.422	27.491	38.633	1.00 46.23	6 6
40	MOTA	1920		PHE I		•	26.545	28.682	38.450	1.00 47.55	6
	ATOM	1921	CD:	l PHE I	3 35		25.230	28.536	38.035	1.00 48.89	6
	MOTA	1922	CD2	2 PHE I			27.056	29.968		1.00 48.56 1.00 47.34	6
	MOTA	1923		1 PHE			24.434	29.653	37.771	1.00 47.34	6
	MOTA	1924	CE	2 PHE 1			26.269	31.087	38.343		6
45	MOTA	1925	CZ	PHE 1			24.958	30.927	37.926	1.00 47.81 1.00 49.37	6
	MOTA	1926		PHE 1			29.224		37.595	1.00 49.37	8
	MOTA	1927		PHE	_		29.020	24.880	37.833		7
	MOTA	1928	N	ILE			30.434		37.530		6
	MOTA	1929					31.634		37.706		6
50	ATOM	1930					32.641				6
	ATOM	1931			_		33.858		36.717	_	6
	MOTA	1932			_		31.966		35.224		6
	MOTA	1933		1 ILE			31.393				
	MOTA	1934		ILE			32.284				8
55	ATOM	1935		ILE			32.977				
	MOTA	1936		ASN			32.068				
	MOTA	1937					32.678				
	MOTA	1938					34.200			_	
	MOTA						34.900				
60	MOTA			1 ASN			34.518				
	MOTA	194	1 NE	2 ASN	в 37		35.942	26.572	41.862	, 1.00 40.33	,

	WO 01/5	8951					PCT/EP01/01457				
							-104				
	ATOM	1942	С	ASN	R	37	32.222	29.077	41.322	1.00 45.58	6
	ATOM	1943		AŚN		37	31.767	29.931	40.566	1.00 44.62	8
	ATOM	1944	N	ILE		38	32.335	29.248	42.635	1.00 45.83	7
	ATOM	1945	CA	ILE		38	31.973	30.489	43.301	1.00 47.98	6
5	ATOM	1946	CB	ILE		38	30.781	30.287	44.214	1.00 46.41	6
-	ATOM	1947		ILE		38	30.510	31.550	44.976	1.00 46.45	6
	MOTA	1948	CG1	ILE	В	38	29.567	29.905	43.356	1.00 47.23	6
	MOTA	1949	CD1	ILE	В	38	28.365	29.406	44.105	1.00 48.96	6
_	MOTA	1950	С	ILE	В	38	33.221	30.805	44.086	1.00 50.65	6
10	ATOM	1951	0	ILE		38	33.546	30.109	45.040	1.00 52.37	8
	MOTA	1952	N	LEU		39	33.926	31.855	43.668	1.00 52.96	7
	MOTA	1953	CA	LEU		39	35.207	32.214	44.264	1.00 53.68	6
	MOTA	1954	CB	LEU		39	36.137	32.698	43.157	1.00 53.70 1.00 53.99	6 6
15	MOTA	1955	CG	LEU		39	36.204	31.706	42.000 40.904	1.00 53.99	6
15	MOTA	1956 1957		LEU		39 39	37.099 36.718	32.257 30.364	42.510	1.00 51.88	6
	ATOM ATOM	1957	CD2	LEU		39	35.272	33.188	45.418	1.00 54.85	6
	ATOM	1959	0	LEU		39	36.061	32.994	46.342	1.00 55.07	8
	ATOM	1960	. <b>M</b>	GLU		40	34.489	34.255	45.359	1.00 55.18	7
20	ATOM	1961	CA	GLU		40	34.509	35.220	46.446	1.00 58.32	6
_•	ATOM	1962	СВ	GLU		40	35.423	36.400	46.144	1.00 59.68	6
	MOTA	1963	CG	GLU	В	40	36.879	36.041	46.018	1.00 65.11	6
	MOTA	1964	CD	GLU	В	40	37.749	37.271	45.846	1.00 69.72	6
	MOTA	1965		GLU		40	37.534	38.034	44.867	1.00 72.04	8
25	MOTA	1966	OE2	GLU		40	38.648	37.477	46.693	1.00 70.63	8
	MOTA	1967	C	GLU		40	33.128	35.738	46.685	1.00 59.54	6
	MOTA	1968	0	GLU		40	32.393	36.057	45.747	1.00 59.65 1.00 60.26	8 7
	ATOM	1969	N	VAL		41 41	32.772 31.468	35.816 36.304	47.956 48.323	1.00 58.68	6
30	MOTA MOTA	1970 1971	CA CB	VAL VAL		41	30.599	35.159	48.862	1.00 59.00	6
30	MOTA	1971		VAL		41	29.318	35.711	49.450	1.00 61.18	6
	ATOM	1973		VAL		41	30.279	34.186	47.740	1.00 59.58	6
	MOTA	1974	C	VAL		41	31.666	37.368	49.379	1.00 58.15	6
	ATOM	1975	0	VAL		41	32.594	37.290	50.187	1.00 56.97	8
35	ATOM	1976	N	ASN	В	42	30.811	38.383	49.337	1.00 58.17	7
	ATOM	1977	CA	ASN	В	42	30.863	39.466	50.302	1.00 58.74	6
	ATOM	1978	CB	ASN		42	31.609	40.673	49.730	1.00 58.84	6
	ATOM	1979	CG	ASN		42	31.962	41.702	50.795	1.00 58.68	6
40	MOTA	1980		ASN		42	31.122	42.100	51.593	1.00 58.91	8 7
40	MOTA	1981		ASN		42	33.215 29.412	42.138 39.823	50.806 50.577	1.00 58.72 1.00 60.60	6
	ATOM ATOM	1982 1983	C	ASN ASN		42 42	28.738	40.457	49.747	1.00 60.00	8
	ATOM	1984	<b>И</b>	GLU		43	28.926	39.401	51.742	1.00 61.86	7
	ATOM	1985	CA	GLU		43	27.543	39.669	52.111	1.00 62.81	6
45	ATOM	1986	СВ	GLU		43	27.117	38.760	53.267	1.00 64.87	6
	ATOM	1987	CG	GLU		43	25.640	38.871	53.591	1.00 67.01	6
	MOTA	1988	CD	GLU		43	25.152	37.779	54.525	1.00 69.52	6
	ATOM	1989	OE1	GLÜ	В	43	23.973	37.842	54.945	1.00 68.10	8
	MOTA	1990		GLU		43	25.944	36.854	54.831	1.00 70.46	8
50	ATOM	1991	C	GLU		43	27.332	41.132	52.476	1.00 60.60	6
	ATOM	1992	0	GLU		43	26.223	41.649	52.387	1.00 59.23 1.00 60.18	8
	ATOM	1993	N	ILE		44	28.408 28.356	41.792 43.199	52.882 53.254	1.00 61.54	7 6
	MOTA MOTA	1994 1995	CA CB	ILE		44 44	29.674	43.199	53.254	1.00 62.98	6
55	ATOM	1996	CG2			44	29.601	45.172	54.183	1.00 61.14	6
	ATOM	1997	CG1			44	29.950	42.877	55.194	1.00 63.64	6
	ATOM	1998	CD1			44	29.004	43.205	56.335	1.00 65.05	6
	MOTA	1999	C	ILE		44	28.141	44.069	52.016	1.00 62.14	6
	MOTA 🗻	2000	0	ILE	В	44	27.318	44.992	52.024	1.00 62.54	8
60	MOTA	2001	N	THR		45			50.959	1.00 60.63	7
	MOTA	2002	CA	THR	В	45	28.806	44.527	49.721	1.00 59.11	6

	WO 01/5	8951								PCT/EP01/01	1457
							-105				
	ATOM	2003	СВ	THR :	В	45	30.190	44.696	49.090	1.00 58.49	6
	ATOM	2004		THR :		45	30.749	43.403	48.815	1.00 60.11	8
	ATOM	2005	CG2	THR		45	31.106	45.444	50.036	1.00 56.17	6
	ATOM	2006	С	THR		45	27.879	43.894	48.688	1.00 58.30	6
5	ATOM	2007	0	THR	В	45	27.555	44.521	47.675	1.00 58.45	8
	MOTA	2008	N	ASN	В	46	27.450	42.660	48.933	1.00 56.14	7
	ATOM	2009	CA	ASN		46	26.560	42.001	47.986	1.00 55.54	6
	MOTA	2010	CB	ASN		46	25.242	42.770	47.894	1.00 54.26	6
4.0	MOTA	2011	CG	ASN		46	24.161	42.171	48.767 49.103	1.00 56.06 1.00 55.63	6 8
10	MOTA	2012		ASN		46	23.195	42.835 40.898	49.103	1.00 56.99	7
	MOTA	2013	ND2 C	ASN ASN		46 46	24.314 27.190	41.867	46.591	1.00 54.59	6
	MOTA	2014 2015	0	ASN		46	26.589	42.228	45.574	1.00 52.67	8
	ATOM ATOM	2015	N	GLU		47	28.408	41.337	46.565	1.00 53.06	7
15	ATOM	2017	CA	GLU		47	29.141	41.131	45.330	1.00 51.52	6
	ATOM	2018	CB	GLU		47	30.320	42.090	45.267	1.00 49.41	6
	ATOM	2019	CG	GLU		47	29.902	43.534	45.211	1.00 51.44	6
	MOTA	2020	CD	GLU		47	31.084	44.472	45.232	1.00 53.91	6
	ATOM	2021		GLU		47	32.183	44.015	44.862	1.00 51.27	8
20	ATOM	2022	OE2	GLU	В	47	30.911	45.662	45.604	1.00 58.92	8
	ATOM	2023	С	GLU		47	29.627	39.697	45.262	1.00 50.23	6
	ATOM	2024	0	GLU		47	30.100	39.150	46.245	1.00 50.97 1.00 50.68	8 7
	MOTA	2025	N	VAL		48	29.509 29.928	39.090 37.706	44.091 43.909	1.00 50.46	6
25	MOTA	2026 2027	CA CB	VAL VAL		48 48	28.712	36.793	43.633	1.00 49.57	6
20	ATOM ATOM	2027		VAL		48	29.162	35.370	43.440	1.00 53.01	6
	ATOM	2029		VAL		48	27.749	36.861	44.781	1.00 50.46	6
	ATOM	2030	C	VAL		48	30.910	37.554	42.757	1.00 49.70	6
	ATOM	2031	0	VAL		48	30.785	38.204	41.727	1.00 50.33	8
30	MOTA	2032	N	ASP	В	49	31.891	36.688	42.950	1.00 48.84	7
	MOTA	2033	CA	ASP		49	32.888		41.935	1.00 49.56	6
	MOTA	2034	CB	ASP		49	34.283	36.610	42.514	1.00 51.66 1.00 50.41	6 6
	ATOM	2035	CG	ASP		49	35.320		41.456 40.443	1.00 50.41	8
35	ATOM	2036 2037		ASP ASP		49 49	35.214 36.240		41.639	1.00 51.65	8
30	MOTA MOTA	2037	C	ASP		49	32.648		41.590	1.00 49.62	6
	ATOM	2039	Ö	ASP		49	32.973		42.364	1.00 49.38	8
	ATOM	2040	N	VAL		50	32.078		40.416	1.00 49.68	7
	ATOM	2041	CA	VAL	В	50	31.721		39.982	1.00 48.91	6
40	MOTA	2042	CB	VAL		50	30.168		40.000	1.00 50.39	6
	MOTA	2043		VAL		50	29.565		38.807	1.00 47.68	6
	MOTA	2044		VAL		50	29.767		40.006	1.00 52.12 1.00 47.99	6 6
	MOTA	2045	C	VAL		50	32.241 32.533		38.598 37.758	1.00 47.55	8
45	MOTA	2046 2047	O N	VAL VAL		50 51	32.349		38.383	1.00 45.73	7
45	ATOM ATOM	2047	CA	VAL		51	32.802		37.116	1.00 44.16	6
	ATOM	2049	CB	VAL		51	34.037		37.313	1.00 43.78	6
	ATOM	2050		VAL		51	34.324		36.031	1.00 40.41	6
	ATOM	2051		VAL		. 51	35.245	31.005	37.728	1.00 40.89	6
50	ATOM	2052	C	VAL		51	31.673		36.569	1.00 45.01	6
	MOTA	2053	0	VAL		51	31.075		37.318	1.00 48.28	8
	MOTA	2054	N	PHE		52	31.382		35.275	1.00 42.51 1.00 41.24	7 6
	ATOM	2055	CA	PHE		52 52	·30.307 28.981		34.708 34.993	1.00 41.24	6
55	ATOM	2056 2057	CB CG	PHE PHE		52 52	28.876		34.394	1.00 42.31	6
J	MOTA ATOM	2057		ene PHE		52	28.448		33.088	1.00 42.63	6
	ATOM	2059		2 PHE		52	29.248		35.123	1.00 43.12	6
	ATOM	2060		LPHE		52	28.394		32.521	1.00 43.87	6
	· ATOM	2061	CE	2 PHE	В	52	29.197		34.562	1.00 43.32	6
60	MOTA	2062	CZ	PHE		52	28.770		33.261	1.00 43.87	6
	MOTA	2063	С	PHE	В	52	30.463	29.345	33.217	1.00 43.44	6

	· WO 01/5	•				PCT/EP01/01457					
				•			106				
		0054	_		_		-106	20 000	22 505	1 00 16 06	0
	ATOM	2064 2065	0	PHE		52 53	31.264 29.692	30.008 28.428	32.585 32.655	1.00 46.26 1.00 44.90	8 7
	ATOM	2065	N	TRP TRP		53	29.725	28.188	31.223	1.00 47.46	6
	ATOM	2067	CA	TRP		53	29.655	26.698	30.907	1.00 47.31	6
5	ATOM	2067	CB CG	TRP		53	30.869	25.949	31.278	1.00 47.31	6
J	ATOM	2069		TRP		53	31.029	24.535	31.246	1.00 49.30	6
	ATOM ATOM	2009		TRP		53	32.342	24.253	31.686	1.00 30.82	6
		2070		TRP		53	30.189	23.473	30.887	1.00 49.80	6
	ATOM ATOM	2071		TRP		53	32.057	26.463	31.719	1.00 50.05	6
10	ATOM	2072				53	32.947	25.448	31.968	1.00 50.03	7
	ATOM	2074	CZ2	TRP		53	32.835	22.955	31.779	1.00 50.23	6
	ATOM	2075	CZ3	TRP		53	30.676	22.182	30.977	1.00 49.78	6
	ATOM	2075	CH2	TRP		53	31.990	21.932	31.421	1.00 50.88	6
	ATOM	2077	C	TRP		53	28.516	28.860	30.619	1.00 48.93	6
15	MOTA	2078	Ö	TRP		53		28.490	30.912	1.00 48.69	8
	ATOM	2079	N	GLN		54	28.746	29.846	29.770	1.00 50.46	7
	ATOM	2080	CA	GLN		54	27.643		29.155	1.00 51.66	6
	ATOM	2081	CB	GLN		54	28.036	31.984	28.844	1.00 51.35	6
	ATOM	2082	CG	GLN		54	26.871	32.851	28.407	1.00 53.49	6
20	ATOM	2083	CD	GLN	В	54	27.117	34.326	28.693	1.00 57.50	
	MOTA	2084	OE1	GLN		54	27.399	34.711	29.837	1.00 57.95	8
	MOTA	2085	NE2	GLN	В	54	27.016	35.161	27.659	1.00 58.04	7
	ATOM	2086	С	GLN	В	54	27.273	29.790	27.898	1.00 52.38	6
	ATOM	2087	0	GLN	В	54	27.564	30.209	26.786	1.00 54.42	8
25	ATOM	2088	N	GLN	В	55	26.638	28.650	28.101	1.00 52.78	7
	MOTA	2089	CA	GLN	В	55	26.203	27.793	27.017	1.00 53.84	6
	MOTA	2090	CB	GLN	В	55	25.672	26.501	27.623	1.00 58.14	6
	MOTA	2091	CG	GLN		55	24.985	25.549	26.663	1.00 66.74	6
	ATOM	2092	CD	GLN		55	24.756	24.190	27.315	1.00 70.87	6
30	MOTA	2093		GLN		55	24.456	24.108	28.528	1.00 73.46	8
	MOTA	2094		GLN		55	24.897	23.117	26.527	1.00 69.32	7
	ATOM	2095	С	GLN		55	25.145	28.495	26.168	1.00 51.37	6
	MOTA	2096	0	GLN		55	23.993	28.631	26.563	1.00 52,24	8
0.5	ATOM	2097	N	THR		56	25.558	28.935	24.989	1.00 48.92	7
35	ATOM	2098	CA	THR		56	24.690	29.660	24.083	1.00 47.03	6
	ATOM	2099	CB	THR		56	25.307	31.018	23.741	1.00 47.18	6
	ATOM	2100 2101		THR		56	25.758 24.291	31.647 31.909	24.946 23.056	1.00 46.91 1.00 45.50	8 6
40	MOTA			THR THR		56 56	24.466	28.896	22.787	1.00 45.50	6
	ATOM ATOM	2102 2103	C O	THR		56	25.351	28.202	22.306	1.00 46.60	8
	ATOM	2103	N	THR		57	23.273	29.034	22.220	1.00 45.86	7
	ATOM	2105	CA	THR	_	57	22.942	28.350	20.984	1.00 44.53	6
	ATOM	2106	CB	THR		57	22.320	26.958	21.247	1.00 44.84	6
	ATOM	2107		THR		57	23.271	26.115	21.910	1.00 41.11	8
45	ATOM	2108		THR		57	21.942	26.306	19.936	1.00 46.63	6
	ATOM	2109	С	THR		57	21.967	29.152	20.162	1.00 43.27	.6
	ATOM	2110	0	THR		57	21.106	29.825	20,700	1.00 44.01	8
	MOTA	2111	N	TRP		58	22.122	29.086	18.849	1.00 41.40	7
	ATOM	2112	CA	TRP	В	58	21.235	29.792	17.945	1.00 42.18	6
50	ATOM	2113	CB	TRP	В	58	21.500	31.302	17.968	1.00 40.63	6
	MOTA	2114	CG	TRP	В	58	22.800	31.729	17.377	1.00 40.64	6
	ATOM	2115		TRP		58	24.048	31.827	18.054	1.00 37.47	6
55	ATOM	2116		TRP		58	24.998	32.252	17.113	1.00 37.44	6
	MOTA	2117		TRP		58	24.456	31.594	19.371	1.00 37.69	6
	ATOM	2118		TRP		58	23.036	32.088	16.087	1.00 39.23	6
	MOTA	2119		TRP		58	24.354	32.404	15.917	1.00 36.19	7
	MOTA	2120		TRP		58	26.336	32.452	17.444	1.00 40.36	6
60	ATOM	2121		TRP		58	25.778	31.789	19.701	1.00 38.85	6
	ATOM	2122		TRP		58	26.708	32.215	18.742	1.00 40.16	6
	ATOM	2123	C	TRP		58 58	21.430	29.217	16.561	1.00 43.00 1.00 44.24	6
	ATOM	2124	0	TRP	Ð	58	22.226	28.320	16.383	1.00 44.24	8

	WO 01/58	8951										PCT/EP01/01457			
							-107		,	•					
	ATOM	2125	N	SER	B	59	20.711	29.729	15.579	1 00	47.57	7			
	ATOM	2126	CA	SER		59	20.814	29.181	14.246		50.36	6			
	ATOM	2127	CB	SER		59	19.517	28.410	13.937		52.43	6			
	ATOM	2128	OG	SER		59	19.677	27.455	12.901		58.14	8			
5	ATOM	2129	С	SER	В	59	21.073	30.250.	13.191		51.80	6			
	MOTA	2130	Ο.	SER	B	59	20.440	31.307	13.184		48.66	8			
	MOTA	2131	N	ASP		60	22.018	29.954	12.303		53.93	7			
10	MOTA	2132	CA	ASP		60	22.393	30.844	11.206		56.01	6			
	MOTA	2133	CB	ASP		60	23.766	31.462	11.474		57.13	6			
	ATOM	2134	CG	ASP		60	24.163	32.503	10.437		58.21	6			
	ATOM	2135		ASP		60	23.714	32.413	9.275		56.08 59.82	8 8			
	ATOM	2136		ASP		60 60	24.952 22.453	33.407 29.976	10.786 9.953		57.25	6			
	ATOM ATOM	2137 2138	С 0	ASP ASP		60	23.458	29.376	9.683		57.02	8			
15	ATOM	2139	N	ARG		61	21.370	29.979	9.192		59.51	7			
	ATOM	2140	CA	ARG		61	21.281	29.171	7.981		62.14	6			
	ATOM	2141	CB	ARG		61	19.852	29.202	7.418		65.88	6			
	ATOM	2142	CG	ARG		61	18.842	28.288	8.125		71.80	6			
	ATOM	2143	CD	ARG		61	17.562	28.189	7.282	1.00	79.30	6			
20	ATOM	2144	NE	ARG	В	61	16.561	27.245	7.806		85.93	7			
	ATOM	2145	CZ	ARG	В	61	15.393	26.967	7.210	1.00	88.02	6			
	MOTA	2146	NH1	ARG	В	61	15.059	27.553	6.059		89.55	7			
	MOTA	2147		ARG		61	14.550	26.101	7.762		88.72	7			
~-	MOTA	2148	C	ARG		61	22.256	29.537	6.868		61.20	6			
25	MOTA	2149	0	ARG		61	22.488	28.725	5.972		61.95	8			
	ATOM	2150	N	THR		62	22.819	30.742	6.898		59.72	7			
	ATOM	2151	CA	THR		62 62	23.755 24.072	31.133 32.653	5.846 5.878		59.39 61.53	6 6			
	ATOM ATOM	2152 2153	CB OG1	THR		62	24.790	32.933	7.077		62.67	8			
30	ATOM	2153	CG2	THR		62	22.783	33.461	5.826		61.46	6			
00	ATOM	2155	C	THR		62	25.055	30.355	5.992		58.40	6			
	ATOM	2156	Ö	THR		62	25.923	30.410	5.129		58.95	8			
	ATOM	2157	N	LEU		63	25.176	29.626	7.095	1.00	57.74	7			
	ATOM	2158	CA	LEU		63	26.365	28.831	7.381	1.00	55.00	6			
35	ATOM	2159	CB	LEU	В	63	26.677	28.871	8.880		53.55	6			
	MOTA	2160	CG	LEU		63	26.908	30.230	9.531		52.72	6			
	MOTA	2161		LEU		63	27.061	30.070	11.038		53.77	6			
	MOTA	2162		LEU		63	28.141	30.866	8.929	1.00	52.77	6			
40	ATOM	2163	C	LEU		63	26.163	27.377 26.624	6.971		54.84 55.28	6 8			
40	MOTA	2164	0	LEU		63	27.125 24.911	26.624	6.858 6.767		53.09	7			
	ATOM ATOM	2165 2166	N CA	ALA ALA		64 64	24.579	25.621	6.403		54.25	6			
	MOTA	2167	CB	ALA		64	23.078		6.274		54.84	6			
	ATOM	2168	C	ALA		64	25.235		5.116		54.35	6			
45	MOTA	2169	Ö	ALA		64	25.441	25.973	4.208		56.81	8			
	ATOM	2170	Ŋ	TRP		65	25.543	23.884	5.040	1.00	50.85	7			
	ATOM	2171	CA	TRP		65	26.148	23.305	3.851	1.00	50.36	6			
	ATOM	2172	CB	TRP	В	65	27.674		3.895		47.85	6			
	ATOM	2173	CG	TRP		65	28.356		4.836		44.59	6			
50	MOTA	2174		TRP		65	28.626		6.229		42.42	6			
	MOTA	2175		TRP		65	29.244		6.711		41.31	6			
55	ATOM	2176		TRP		65	28.406		7.115		39.86 43.65	6 6			
	ATOM	2177		TRP		65 65	28.809 29.344		4.544 5.662		42.95	7			
	ATOM ATOM	2178 2179		TRP TRP		65	29.544		8.041		41.27	6			
	ATOM	2179		TRP		65	28.807		8.439		39.24	6			
	ATOM	2181		TRP		65	29.419		8.886		40.26	6			
	ATOM	2182	C	TRP		65	25.751		3.839		51.92	6			
60	ATOM	2183	Ö	TRP		65	25.269	21.312	4.846	1.00	51.65	8			
	ATOM	2184	N	ASN		66	25.933	21.173	2.703		54.28	7			
	MOTA	2185	CA	ASN	В	66	25.579	19.760	2.599	1.00	56.88	6			

	WO 01/5	8951									PCT	<b>/EP01/0</b> 1	1457
								-108					
	ATOM	2186	СВ	ASN	R A	56		25.361	19.349	1.139	1 00	59.16	6
	ATOM	2187	CG	ASN		56		25.067	17.869	1.006		62.92	. 6
	ATOM	2188		ASN		56		25.084	17.308	-0.090		64.20	. 8
	ATOM	2189		ASN		56		24.792	17.223	2.138		63.82	7
5	ATOM	2190	С	ASN		56		26.684	18.903	3.197		56.22	6
	ATOM	2191	0	ASN		66		27.826	18.942	2.747	1.00	54.74	8
	ATOM	2192	N	SER	в 6	67	;	26.336	18.112	4.200		57.45	7
	MOTA	2193	CA	SER		67		27.323	17.276	4.866		60.21	· 6
	ATOM	2194	CB	SER		67		27.251	17.503	6.376		60.70	6
10	MOTA	2195	OG	SER		67		25.956	17.197	6.844		59.26	8
	MOTA	2196	C	SER		67		27.139	15.796			60.90	6
	MOTA	2197	0	SER		67		27.705	14.926	5.221		59.74	8
	ATOM	2198	N	SER		68		26.350	15.519	3.528		62.89	7
15	ATOM	2199	CA	SER		68 68		26.094 25.141	14.148 14.127	3.129 1.933		64.44	6 6
13	ATOM ATOM	2200 2201	CB OG	SER SER		68		25.569	15.023	0.923		65.05	8
	ATOM	2201	C	SER		68		27.399	13.437	2.790		65.22	6
	ATOM	2202	o	SER		68		27.491	12.215			65.18	8
	ATOM	2204	N	HIS		69		28.414	14.203	2.401		66.21	7
20	ATOM	2205	CA	HIS		69		29.702	13.617		_	66.70	6
	MOTA	2206	СВ	HIS		69		29.832	13.502	0.539	1.00	69.64	6
	ATOM	2207	CG	HIS	в (	69		29.047	12.363	-0.025	1.00	74.89	6
	ATOM	2208	CD2	HIS	В (	69		29.433	11.123	-0.417	1.00	76.05	6
	MOTA	2209		HIS		69		27.673	12.393	-0.143		76.35	7
25	MOTA	2210		HIS		69		27.245	11.221	-0.583		76.49	6
	MOTA	2211		HIS		69		28.293	10.433	-0.757		76.65	7
	ATOM	2212	C	HIS		69		30.895	14.352			65.56	6
	ATOM	2213	0	HIS		69		31.919	14.538			63.93	8
30	ATOM	2214	N	SER		70 70		30.746	14.737			65.07 63.00	7 6
30	MOTA MOTA	2215 2216	CA CB	SER SER		70 70		31.772 31.954	15.463 16.854			61.97	6
	ATOM	2217	OG	SER		70		30.716	17.393	3.551		59.22	8
	ATOM	2218	C	SER		70		31.353	15.576			62.92	6
	ATOM	2219	Ö	SER		70		30.288	15.077			62.73	8
35	ATOM	2220	N	PRO		71		32.204	16.199			62.42	7
	ATOM	2221	CD	PRO		71		33.624	16.490		1.00	61.13	6
	ATOM	2222	CA	PRO	В	71		31.901	16.371	8.361	1.00	61.29	6
	MOTA	2223	CB	PRO	В	71		33.124	17.103			,61.30	6
	MOTA	2224	CG	PRO		71		34.214	16.490			60.40	. 6
40	ATOM	2225	С	PRO		71		30.619	17.159			61.12	6
	ATOM	2226	0	PRO		71		30.222	17.964			60.52	8
	ATOM	2227	N	ASP		72		29.973	16.916			62.69	7
	MOTA	2228 2229	CA	ASP		72 72		28.714 27.839	17.587 16.649			62.55 64.34	6 6
45	ATOM ATOM	2230	CB CG	ASP ASP		72 72		27.833	15.613			67.53	6
	ATOM	2231		ASP		72		25.937	15.794			67.60	8
	ATOM	2232		ASP		72		27.808	14.627			70.97	8
	ATOM	2233	C	ASP		72		28.962	18.858			60.43	6
	ATOM	2234	0	ASP		72		28.137	19.780		1.00	58.20	8
50	ATOM	2235	N	GLN	В	73		30.123	18.883	11.483	1.00	58.87	7
	ATOM	2236	CA	GLN		73		30.549	19.981			58.03	6
	ATOM	2237	CB	GLN		73		30.400	19.583			60.56	6
	ATOM	2238	CG	GLN		73		29.025	19.532			62.56	6
55	MOTA	2239	CD CD1	GLN		73 73		29.096	19.033			64.10	6
55	MOTA	2240		GLN		73 73		29.599	17.945			67:42 65.84	8
	ATOM ATOM	2241 2242	NE2 C	GLN GLN		73 73		28.628 31.998	19.830 20.392			55.43	7 6
	ATOM	2242	0	GLN		73 73		32.845	19.591			56.41	8
	ATOM	2244	N	VAL		74		32.275	21.642			50.91	7
60	ATOM	2245	CA	VAL		74		33.621	22.197			48.23	6
	MOTA	2246	CB	VAL		74		33.925	22.849		1.00	46.99	6

	WO 01/58	8951								PCT/	<b>EP</b> 01/01	457
		•					-109					
	7 DOM	2247	CC1	VAL 1	2	74	34.009	21.782	10.026	1.00 4	48.63	6
	ATOM ATOM	2247		VAL		74	32.864	23.871	10.777	1.00 4		6
	ATOM	2249	C	VAL		74	33.734	23.259	13.532	1.00 4		6
	MOTA	2250	o	VAL 1		74	32.731	23.812	13.964	1.00 4		8
5	ATOM	2251	N	SER		75	34.951	23.524	13.980	1.00 4		7
Ū	ATOM	2252	CA	SER !		75	35.177	24.551	14.982	1.00	41.30	6
	ATOM	2253	CB	SER		75	36.314	24.145	15.920	1.00	39.05	б
	ATOM	2254	OG	SER		75	35.850	23.290	16.932	1.00	30.94	. 8
	ATOM	2255	C	SER :		75	35.513	25.856	14.264	1.00	40.02	6
10	ATOM	2256	0	SER	В	75	36.478	25.936	13.516	1.00		8
	MOTA	2257	N	VAL	В	76	34.701	26.875	14.497	1.00		7
	MOTA	2258	CA	VAL :	В	76	34.885	28.167	13.861	1.00		6
	ATOM	2259	CB	VAL		76	33.607	28.580	13.124	1.00		6
	MOTA	2260		VAL		76	33.788	29.928	12.483	1.00		6
15	ATOM	2261		VAL		76	33.244	27.539	12.090	1.00		6
	MOTA	2262	С	VAL		76	35.218	29.256	14.861	1.00		6
	MOTA	2263	0 ·	VAL		76	34.626	29.322	15.926	1.00		8 7
	MOTA	2264	N	PRO		77	36.188	30.120	14.541	1.00		6
00	ATOM	2265	CD	PRO		77	37.176	30.053	13.460 15.479	1.00		6
20	MOTA	2266	CA	PRO		77	36.527 37.717	31.189 31.853	14.816	1.00		6
	ATOM	2267	CB	PRO PRO		77 77	38.342	30.728	14.078	1.00		6
	MOTA	2268 2269	CG C	PRO		77	35.346	32.141	15.622	1.00		6
	ATOM ATOM	2270	0	PRO		77	34.663	32.438	14.658	1.00		8
25	ATOM	2271	N	ILE		78	35.105	32.600	16.835	1.00		7
20	ATOM	2272	CA	ILE		78	34.018	33.515	17.129	1.00		6
	ATOM	2273	CB	ILE		78	34.107	33.946	18.602	1.00	41.86	6
	ATOM	2274	CG2			78	33.311	35.183	18.861		40.86	6
	ATOM	2275		ILE		78	33.622	32.799	19.469	1.00	45.04	6
30	ATOM	2276	CD1	ILE	В	78	32.313	32.232	18.983		46.64	6
	ATOM	2277	С	ILE	В	78	34.000	34.741	16.231		41.00	6
	ATOM	2278	0	ILE	В	78	32.947	35.225	15.846		41.00	8
	MOTA	2279	N	SER	В	79	35.185	35.227	15.898		43.87	7
	MOTA	2280	CA	SER		79	35.368	36.399	15.047		44.52	6
35	ATOM	2281	CB	SER		79	36.842	36.792	15.061		46.91	6 8
	ATOM	2282	OG	SER		79	37.657	35.687	14.696		49.85	6
	ATOM	2283	C	SER		79	34.914	36.244 37.228	13.593 12.876		43.49	8
	ATOM	2284	0	SER SER		79 80	34.805 34.656	35.016	13.160		43.24	7
40	ATOM	2285	N ĊA	SER		80	34.227	34.769	11.793		44.14	. 6
40	MOTA MOTA	2286 2287	CB	SER		80	34.955	33.552	11.221		44.85	6
	ATOM	2288	OG	SER		80	36.354	33.781	11.115		52.06	8
	ATOM	2289	C	SER		80	32.731	34.545	11.690	1.00	44.49	6
	ATOM	2290	ō	SER		80	32.213	34.308	10.609	1.00	44.54	8
45	ATOM	2291	N	LEU		81	32.039	34.625	12.820		45.89	7
	ATOM	2292	CA	LEU	В	81	30.589	34.418	12.858		45.78	6
	ATOM	2293	CB	LEU	В	81	30.250	33.187	13.700		42.48	6
	MOTA	2294	CG	LEU		81	30.945	31.867	13.420		42.60	6
	ATOM	2295		. LEU		81	30.769	30.949	14.584		41.27	6
50	ATOM	2296		LEU		81	30.379	31.266	12.165		45.70	6
	ATOM	2297	С	LEU		81	29.909	35.611	13.513		45.11	6
	ATOM	2298	0	LEU		81	30.562	36.439	14.154		46.02 42.92	8 7
	ATOM	2299	N ~-	TRP		82	28.596	35.696	13.344		40.24	6
EE	ATOM	2300	CA	TRP		82	27.829 26.493	36.737 36.962	13.984 13.290		42.22	6
55	MOTA	2301	CB CG	TRP TRP		82 82	25.535	37.766	14.126		43.85	6
	MOTA ATOM	2302 2303		TRP		82	24.580	37.700	15.072		44.14	6
	ATOM	2304	CE2			82	23.972	38.369	15.687		42.05	6
	ATOM	2305	CE			82	24.185	35.964	15.461		42.43	6
60	ATOM	2306		LTRP		82	25.459	39.118	14.204		.42.92	6
	ATOM	2307		l TRP		82	24.527	39.490	15.138	1.00	41.43	7

WO 01/5	8951								PCT/EP01/01	1457
						-110			•	
ATOM	2308	CZ2	TRP	В	82	22.991	38.238	16.671	1.00 42.94	6
ATOM	2309	CZ3	TRP	В	82	23.211	35.832	16.442	1.00 41.79	6
ATOM	2310	CH2	TRP	В	82	22.625	36.965	17.036	1.00 42.57	6
ATOM	2311	С	TRP	В	82	27.579	36.100	15.323	1.00 39.43	6
ATOM	2312	0	TRP	В	82	27.379	34.904	15.410	1.00 41.05	8
ATOM	2313	N	VAL	В	83	27.594	36.892	16.373	1.00 41.18	7
MOTA	2314	CA	VAL	В	83	27.363	36.359	17.699	1.00 40.57	6
ATOM	2315	CB	VAL	В	83	28.714	36.210	18.444	1.00 41.00	6 -
MOTA	2316	CG1	VAL	В	83	28.494	35.956	19.903	1.00 45.57	6
ATOM	2317	CG2	VAL	В	83	29.491	35.066	17.856	1.00 40.97	· 6 ·

5 10 1.00 40.40 26.399 37.275 18.460 6 ATOM 2318 С VAL B 83 1.00 42.78 26.424 38.487 18.301 R 2319 VAL B 83 MOTA 0 36.693 1.00 40.62 7 25.510 19.271 MOTA 2320 PRO B 84 N 1.00 43.06 25.296 35.250 19.465 6 MOTA 2321 CD PRO B 84 20.052 1.00 39.62 15 24.540 37.460 б MOTA 2322 CA PRO B 84 23.839 36.384 20.880 1.00 39.00 6 PRO B 84 ATOM 2323 CB 23.899 35.212 20.013 1.00 43.18 6 ATOM 2324 CG PRO B 84 20.937 1.00 37.37 MOTA 2325 C· PRO B 84 25.246 38.474 6 1.00 34.20 26.215 38.140 21.603 2326 PRO B 84 8 MOTA 0 39.706 20.950 1.00 36.29 20 24.753 7 MOTA 2327 N ASP B 85 1.00 37.57 25.341 40.736 21.777 6 ASP B ATOM 2328 CA 85 1.00 38.52 25.112 42.107 21.152 2329 ASP B 6 ATOM CB 85 20.952 1.00 40.81 23.661 42.418 6 ASP B ATOM 2330 CG 85 22.925 41.501 20.578 1.00 41.81 8 2331 ASP B 85 ATOM OD1 25 2332 ASP B 85 23.254 43.579 21.148 1.00 41.12 8 ATOM OD2 1.00 39.08 24.776 40.687 23.193 6 ATOM 2333 С ASP B 85 2334 ASP B 24.261 41.668 23.714 1.00 36.01 8 ATOM 0 85 23.811 1.00 38.19 7 24.902 39.522 ATOM 2335 N LEU B 86 1.00 39.63 6 24.421 39.306 25.161 MOTA 2336 CA LEU B 86 30 24.459 25.502 1.00 37.18 6 37.819 MOTA 2337 CB LEU B 86 LEU B 23.585 36.939 24.621 1.00 38.33 6 2338 86 MOTA CG CD1 LEU B 23.700 35.493 25.065 1.00 33.72 6 2339 86 MOTA 22.159 37.433 24.693 1.00 35.49 6 ATOM 2340 CD2 LEU B 86 MOTA 2341 С LEU B 86 25.223 40.061 26.201 1.00 40.05 6 35 26.065 1.00 42.26 MOTA 2342 0 LEU B 86 26.432 40.251 8 24.541 40.467 27.260 1.00 40.28 7 MOTA 2343 N ALA B 87 25.180 28.339 1.00 40.51 6 MOTA 2344 CA ALA B 87 41.193 25.048 42.698 28.091 1.00 40.62 6 2345 ALA B 87 ATOM ÇВ 24.521 40.826 29.660 1.00 40.28 6 87 MOTA 2346 С ALA B 40 23.306 29.729 1.00 40.56 2347 ALA B 87 40.702 MOTA 0 2348 ALA B 88 25.316 40.634 30.703 1.00 39.13 7 ATOM N 1.00 38.99 24.756 40.340 32.014 6 MOTA 2349 CA ALA B 88 1.00 37.09 25.749 32.850 2350 ALA B 88 39.577 6 MOTA CB 32.665 1.00 40.68 6 2351 ALA B 88 24.433 41.686 MOTA С 45 42.392 - 33.134 1.00 38.34 25.319 8 ALA B MOTA 2352 0 88 23.153 42.033 32.667 1.00 42.45 7 2353 TYR B 89 MOTA N 1.00 44.08 TYR B 89 22.654 43.285 33,232 6 MOTA 2354 CA TYR B 89 21.133 43.209 33.363 1,00.46.62 6 ATOM 2355 CB 20.395 43.055 32.056 1.00 51.23 б ATOM 2356 CG TYR B 89 50 32.036 1.00 54.25 CD1 TYR B 89 19.022 42.816 6 MOTA 2357 30.826 1.00 55.90 ATOM 2358 CE1 TYR B 89 18.322 42.711 6 30.835 1.00 52.13 21.054 43.179 MOTA 2359 CD2 TYR B 89 6 20.366 43.078 29.626 1.00 54.28 CE2 TYR B 6 ATOM 2360 89 19.001 42.847 29.629 1.00 55.97 6 ATOM 2361 CZTYR B 89 55 42.787 28.440 1.00 59.26 MOTA 2362 OH TYR B 89 18.313 8 23.243 43.725 34.579 1.00 43.48 MOTA 2363 С TYR B 89 1.00 42.18 TYR B 89 23.409 44.917 34.820 8 MOTA 2364 0 1.00 42.08 42.784 35.466 2365 ASN B 90 23.540 7 MOTA N 43.155 36.755 1.00 40.43 6 ASN B 90 24.102 ATOM 2366 CA 60 23.262 42.581 37.904 1.00 39.29 6

ASN B

ASN B

2367

2368

CB

CG

ATOM

MOTA

90

90

23.084

41.082 37.824

1.00 40.77

	WO 01/5	58951			,		,			PCT/EP01/0	1457
							-111				
	ATOM	2369	OD1	ASN E	3 :	90	22.778	40.536	36.774	1.00 40.90	8
	MOTA	2370		ASN E		90	23.257	40.412	38.948	1.00 42.41	7
	ATOM	2371	С	ASN E	3	90	25.554	42.768	36.921	1.00 41.50	6
	ATOM	2372	0	ASN E	3	90	26.031	42.618	38.042	1.00 42.85	8
5	MOTA	2373		ALA E		91	26.250	42.605	35.798	1.00 43.60	7
	MOTA	2374		ALA I		91	27.669	42.266	35.811	1.00 43.31	6
	MOTA	2375	CB	ALA I		91	28.156	41.933	34.415	1.00 42.36	6 6
	MOTA	2376	C	ALA I		91	28.359	43.513 44.637	36.336 35.934	1.00 44.47 1.00 43.75	8
40	MOTA	2377	0	ALA I		91 92	28.048 29.295	43.299	37.244	1.00 44.99	7
10	ATOM	2378 2379	N CA	ILE I		92 92	30.009	44.379	37.244	1.00 45.69	6
	ATOM ATOM	2379	CB	ILE I		92	30.052	44.061	39.418	1.00 46.91	6
	ATOM	2381	CG2	ILE 1		92	31.419	43.514	39.831	1.00 49.50	6
	ATOM	2382		ILE I		92	29.726	45.288	40.232	1.00 48.64	6
15	ATOM	2383	CD1	ILE I	В	92	29.920	45.030	41.718	1.00 53.73	6
	MOTA	2384	С	ILE	В	92	31.428	44.532	37.302	1.00 45.86	6
	MOTA	2385	0	ILE :		92	32.156	45.487	37.611	1.00 45.24	8
	MOTA	2386	N	SER :		93	31.804	43.581	36.453	1.00 41.25	7
00	ATOM	2387	CA	SER :		93	33.104	43.578	35.813	1.00 38.58 1.00 35.19	6 6
20	ATOM	2388	CB	SER :		93	34.056	42.662	36.568 36.388	1.00 35.19	8
	ATOM	2389	og	SER		93	33.682 32.852	41.315 43.015	34.431	1.00 33.43	6
	ATOM	2390	C	SER SER		93 93	32.032	42.493	34.174	1.00 39.63	8
	MOTA MOTA	2391 2392	O N	LYS		94	33.815	43,131	33.524	1.00 43.16	7
25	ATOM	2392	CA	LYS		94	33.598	42.557	32.212	1.00 43.98	6
	ATOM	2394	CB	LYS		94	34.355	43.325	31.127	1.00 46.29	6
	MOTA	2395	CG	LYS		94	35.769	43.727	31.434	1.00 50.31	6
	ATOM	2396	CD	LYS	В	94	36.225	44.764	30.401	1.00 52.39	6
	MOTA	2397	CE	LYS	В	94	35.853	44.341	28.978	1.00 52.02	6
30	ATOM	2398	NZ	LYS		94	36.333	45.308	27.965	1.00 54.82	7
	MOTA	2399	C	LYS		94	33.963	41.075	32.230	1.00 43.71	6 8
	ATOM	2400	0,	LYS		94	34.673	40.602	33.114	1.00 44.78 1.00 44.16	7
	MOTA	2401	N	PRO		95 05	33.443 32.562	40.310 40.750	31.267 30.171	1.00 42.37	6
35	ATOM	2402 2403	CD CA	PRO PRO		95 95	33.704	38.873	31.184	1.00 39.82	6
55	ATOM ATOM	2403	CB	PRO		95	32.836	38.422	30.016	1.00 40.83	6
	ATOM	2405	CG	PRO		95	31.813	39.505	29.881	1.00 42.58	6
	ATOM	2406	C	PRO		95	35.141	38.524	30.941	1.00 39.41	6
	ATOM	2407	Ō	PRO		95	35.772	39.048	30.032	1.00 40.47	8
40	MOTA	2408	N	GLU	В	96	35.663	37.637	31.765	1.00 39.61	7
	MOTA	2409	CA	GLU	В	96	37.020	37.175	31.582	1.00 39.82	6
	MOTA	2410	CB	GLU		96	37.765	37.046	32.915	1.00 41.36	6
	MOTA	2411	CG	GLU		96	39.238	36.644	32.763	1.00 50.17	6
AE	ATOM	2412	CD	GLU.		96	39.989	36.540	34.094	1.00 55.05 1.00 57.32	6 8
45	MOTA	2413		GLU		96 06	39.506 41.067	37.129 35.888	35.084 34.153	1.00 57.32	8
	MOTA	2414 2415	C C	GLU		96 96	36.802	35.804	30.966	1.00 39.55	6
	MOTA MOTA	2415	0	GLU		96	36.537	34.840	31.676	1.00 38.71	8
	ATOM	2417	N	VAL		97	36.864	35.736	29.638	1.00 36.87	7
50	MOTA	2418	CA	VAL		97	36.690	34.475	28.938	1.00 35.52	6
•	ATOM	2419	CB	VAL		97	36.457	34.702	27.448	1.00 35.28	6
	ATOM	2420		VAL	В	97	36.249	33.378	26.752	1.00 33.50	6
	ATOM	2421		VAL	В	97	35.249	35.586	27.255	1.00 31.71	6
	ATOM	2422	С	VAL		97	37.935	33.640	29.157	1.00 35.07	6
55	MOTA	2423	0	VAL		97	39.025	34.005	28.741	1.00 37.13	8
	ATOM	2424	N	LEU		98	37.759	32.511	29.823	1.00 35.85	7
	MOTA	2425	CA	LEU		98	38.866	31.631	30.167 31.482	1.00 36.60 1.00 37.34	6 6
	MOTA	2426	CB	LEU LEU		98 98	38.554 38.127	30.913 31.727	32.701	1.00 37.34	6
60	MOTA MOTA	2427 2428	CG CD1	LEU.		98	37.534	30.812	33.739	1.00 37.97	6
50	ATOM	2429		LEU		98	39.306	32.469	33.259	1.00 41.28	6
		-									

	WO 01/5	8951								PCT/EP01/01	1457
							-112				
	ATOM	2430	С	LEU	Þ	98		30.581	29.128	1.00 36.56	6
	ATOM	2431		LEU		98		29.889	29.251	1.00 37.06	8
	ATOM	2432	N	THR		99	38.371	30.467	28.103	1.00 36.66	7
	ATOM	2433	CA	THR		99	38.578	29.438	27.100	1.00 37.03	6
5	ATOM	2434	CB	THR		99	37.405	28.414	27.142	1.00 40.73	6
•	ATOM	2435		THR		99	36.152	29.097	26.972	1.00 42.70	8
	ATOM	2436		THR		99	37.400	27.676	28.466	1.00 37.60	6
	ATOM	2437	C	THR		99	38.725	29.932	25.680	1.00 34.89	6
	MOTA	2438	0	THR	В	99	38.401	31.073	25.378	1.00 35.25	8
10	MOTA	2439	N	PRO	В	100	39.231	29.066	24.786	1.00 35.40	7
	ATOM	2440	CD	PRO	В	100	39.818	27.745	25.056	1.00 33.38	6
	ATOM	2441	CA	PRO			39.413	29.420	23.380	1.00 35.17	6
	ATOM	2442	CB	PRO			39.783	28.095	22.745	1.00 33.58	6
	ATOM	2443	CG	PRO			40.603	27.476	23.789	1.00 34.20	6
15	ATOM	2444	С	PRO			38.107	29.961	22.852	1.00 37.17	6
	ATOM	2445	0	PRO			37.052	29.396	23.103	1.00 38.59	8
	MOTA	2446	N	GLN			38.168	31.066	22.130	1.00 39.08 1.00 40.23	7 6
	MOTA	2447	CA	GLN			36.949	31,636	21.621	1.00 40.23	6.
20	ATOM	2448	CB	GLN			37.071 36.866	33.155 33.742	21.576 22.960	1.00 35.64	6
20	ATOM ATOM	2449 2450	CG CD	GLN GLN			37.334	35.158	23.075	1.00 47.02	6
	ATOM	2451		GLN			36.871	36.035	22.350	1.00 50.05	8
	ATOM	2452		GLN			38.260	35.398	23.997	1.00 45.46	7
	ATOM	2453	C	GLN			36.536	31.057	20.295	1.00 39.08	6
25	ATOM	2454	ō	GLN			36.496	31.747	19.282	1.00 37.88	8
	ATOM	2455	N	LEU			36.212	29.768	20.342	1.00 40.24	7
	ATOM	2456	CA	LEU			35.770	28.997	19.183	1.00 39.64	6
	ATOM	2457	СВ	LEU			36.652	27.759	18.982	1.00 37.23	6
	ATOM	2458	CG	LEU	В	102	38.155	27.988	18.842	1.00 37.24	6
30	MOTA	2459	CD1	LEU	В	102	38.852	26.666	18.659	1.00 33.59	6
	MOTA	2460	CD2	LEU			38.429	28.893	17.665	1.00 36.66	6
	ATOM	2461	С	LEU			34.349	28.528	19.394	1.00 39.73	6
	ATOM	2462	0	LEU			33.948	28.210	20.502	1.00 38.45	8
05	ATOM	2463	N	ALA			33.586	28.492	18.317	1.00 41.12	7
35	ATOM	2464	CA	ALA			32.218	28.017	18.375	1.00 40.48 1.00 39.15	6
	ATOM	2465	CB	ALA			31.271	29.034	17.760 17.599	1.00 39.13	6 6
	ATOM	2466	С	ALA			32.163	26.711 26.337	16.917	1.00 40.28	8
	MOTA MOTA	2467 2468	N O	ALA ARG			33.109 31.045	26.014	17.715	1.00 30.32	7
40	MOTA	2469	CA	ARG			30.876	24.755	17.019	1.00 44.21	6
70	MOTA	2470	CB	ARG			30.557	23.659	18.027	1.00 43.23	6
	ATOM	2471	CG	ARG			30.760	22.273	17.496	1.00 45.99	6
	ATOM	2472	CD	ARG			32.214	21.957	17.217	1.00 44.48	6
	ATOM	2473	NE	ARG			32.306	20.612	16.652	1.00 45.67	7
45	ATOM	2474	CZ	ARG	В	104	33.434	19.985	16.341	1.00 42.29	6
	ATOM	2475	NH1	ARG	В	104 [.]	34.593	20.576	16.534	1.00 40.18	7
	MOTA	2476	NH2	ARG	В	104	33.397	18.755	15.847	1.00 43.70	7
	MOTA	2477	С	ARG			29.736	24.954	16.040	1.00 44.71	6
	MOTA	2478	0	ARG			28.655	25.377	16.425	1.00 43.84	8
50	ATOM	2479	N	VAL			29.990	24.686	14.767	1.00 45.98	7
	ATOM	2480	CA	VAL			28.955	24.862	13.761	1.00 46.86	6
	ATOM	2481	CB	VAL			29.404	25.834	12.663	1.00 43.67 1.00 42.93	6
	ATOM	2482	_	VAL			28.257	26.111 27.116	11.715 13.281	1.00 42.93	6 6
55	ATOM	2483 2484	CGZ	VAL VAL			29.885 28.546	23.546	13.201	1.00 50.58	6
JJ	MOTA MOTA	2484	0	VAL			29.393	22.808	12.589	1.00 51.09	8
	ATOM	2485	N			106		23.266	13.158	1.00 51.24	7
	ATOM	2487	CA			106	26.677	22.056	12.577	1.00 52.00	6
	ATOM	2488	CB	VAL			25.464	21.592	13.387	1.00.52.31	6
60	ATOM	2489		VAL			25.038	20.207	12.931	1.00 52.15	6
	MOTA	2490		VAL			25.798	21.607	14.865	1.00 50.55	6
						•					

	WO 01/5	8951								PCT/EP01/01	457
							-113			•	
	ATOM	2491	С	VAL B	106		26.243	22.369	11.147	1.00 52.00	6
	ATOM	2492	0	VAL B			25.782	23.474	10.870	1.00 52.80	8
	MOTA	2493	N	SER B			26.388	21.401	10.248	1.00 51.28	7
=	ATOM	2494	CA	SER B			26.038	21.592	8.845	1.00 52.41	6
5	MOTA	2495 2496	CB OG	SER B			26.175 25.609	20.272 19,216	8.097 8.855	1.00 54.05 1.00 58.60	6 8
	MOTA MOTA	2490	C	SER B			24.676	22.198	8.544	1.00 52.33	6
	ATOM	2498	0	SER B			24.469	22.728	7.460	1.00 52.31	8
•	ATOM	2499	N	ASP B			23.753	22.132	9.494	1.00 54.48	7
10	MOTA	2500	CA	ASP B			22.417	22.687	9.285	1.00 57.36	6
	ATOM	2501	CB	ASP B	108		21.376	21.830	10.007	1.00 59.13	6
	MOTA	2502	CG	ASP B			21.474	21.933	11.512	1.00 61.77	6
•	ATOM	2503		ASP B			22.604	21.993	12.034	1.00 63.26	8
15	MOTA	2504		ASP B			20.419	21.941 24.152	12.180 9.715	1.00 63.13 1.00 58.76	8 6
15	ATOM ATOM	2505 2506	С 0	ASP B			22.266 21.163	24.152	9.713	1.00 50.78	8
	ATOM	2507	N	GLY B			23.376	24.784	10.087	1.00 59.97	7
	ATOM	2508	CA	GLY B			23.346	26.175	10.489	1.00 58.62	6
	ATOM	2509	C	GLY B			23.213	26.394	11.983	1.00 59.08	6
20	MOTA	2510	0	GLY B	109		23.123	27.534	12.437	1.00 58.71	8
	ATOM	2511	N	GLU B			23.187	25.317	12.758	1.00 58.29	7
	MOTA	2512	CA	GLU B			23.062	25.451	14.202	1.00 57.49	6
	MOTA	2513	CB	GLU B			22.619	24.125	14.827 16.208	1.00 60.94 1.00 64.96	6 6
25	ATOM ATOM	2514 2515	CG CD	GLU B			21.947 20.623	24.234 25.007	16.208	1.00 64.96	6
25	ATOM	2516	OE1	GLU B			20.023	25.007	15.044	1.00 70.48	8
	ATOM	2517		GLU B			20.146	25.493	17.223	1.00 67.90	8
	ATOM	2518	C	GLU B			24.432	25.838	14.723	1.00 56.48	6
	MOTA	2519	0	GLU B	110		25.447	25.291	14.282	1.00 58.51	8
30	MOTA	2520	N	VAL B			24.461	26.780	15.656	1.00 52.94	7
	MOTA	2521	CA	VAL B			25.706	27.254	16.237	1.00.49.98	6
	ATOM	2522	CB	VAL B			25.933	28.743	15.914 16.502	1.00 50.06 1.00 48.91	6 6
	MOTA MOTA	2523 2524		VAL B			27.259 25.894	29.199 28.973	14.406	1.00 48.91	6
35	ATOM	2525	C	VAL B			25.702	27.095	17.749	1.00 49.73	6
	MOTA	2526	ō	VAL B	_	•	24.730	27.431	18.413	1.00 47.85	8
	ATOM	2527	N	LEU B			26.795	26.581	18.292	1.00 49.78	7
	MOTA	2528	CA	LEU B			26.907	26.404	19.733	1.00 50.84	6
40	MOTA	2529	CB	LEU B			26.903	24.914	20.107	1.00 54.21	6
40	MOTA	2530	CG	LEU B			26.075	23.868	19.337	1.00 56.22	6
	ATOM	2531		LEU B			24.673 26.802	24.393 23.504	19.025 18.065	1.00 58.51 1.00 54.95	6 6
	ATOM ATOM	2532 2533	CDZ	LEU B			28.202	27.038	20.242	1.00 54.55	6
	MOTA	2534	Ō	LEU B			29.300	26.651	19.829	1.00 51.33	8
45	ATOM	2535	N	TYR B			28.073	28.013	21,134	1.00 47.63	7
	ATOM	2536	CA	TYR B			29.227	28.681	21.709	1.00 46.01	6
	MOTA	2537	CB	TYR B			29.266	30.154	21.279	1.00 45.50	6
	ATOM	2538	CG	TYR B			30.415	30.970	21.868	1.00 45.48	6
50	MOTA	2539		TYR B			31.715	30.468	21.902	1.00 43.49 1.00 42.81	6 6
50	MOTA MOTA	2540 2541		TYR B			32.766 30.200	31.225 32.262	22.412 22.367	1.00 42.81	6
	ATOM	2542	CE2				31.246	33.022	22.876	1.00 42.75	· 6
	MOTA	2543	CZ	TYR B			32.528	32.499	22.897	1.00 45.11	6
	ATOM	2544	ОН	TYR B			33.579	33.248	23.397	1.00 46.12	8
55	ATOM	2545	С	TYR B	113		29.081	28.561	23.208	1.00 45.62	6
	ATOM	2546	0	TYR B			28.130	29.064	23.783	1.00 48.17	8
	MOTA	2547	N	MET B			30.025	27.887	23.842	1.00 45.82	7
	MOTA MOTA	2548 2549	CA CB	MET B			29.966 29.652	27.691 26.237	25.280 25.578	1.00 47.40 1.00 51.46	6 6
60	MOTA	2550	CG	MET B			29.408	25.958	27.030	1.00 56.47	6
٠,	ATOM	2551	SD	MET B			29.463	24.204	27.290	1.00 61.08	16

	WO 01/58	3951								PCT/EP01/01	1457
							-114				
	ATOM	2552	CE	MET	В	114	27.833	23.732	26.736	1.00 59.81	6
	MOTA	2553	C	MET			31.281	28.060	25.944	1.00 47.40	6
	MOTA	2554	0	MET			32.093	27.187	26.268	1.00 46.46	8
_	MOTA	2555	N	PRO			31.511	29.364	26.158	1.00 46.76	7
5	ATOM	2556	CD	PRO			30.680	30.502	25.712	1.00 45.52	6
	MOTA	2557	CA	PRO			32.744	29.832	26,786	1.00 44.75	6
	ATOM	2558	CB	PRO			32.834	31.259	26.285 26,316	1.00 47.19 1.00 45.23	6 6
	ATOM ATOM	2559 2560	CG C	PRO PRO			31.382 32.653	31.687 29.776	28.303	1.00 45.23	6
10	ATOM	2560	0	PRO			31.567	29.776	28.865	1.00 45.70	8
10	ATOM	2562	N	SER			33.783	29.545	28.965	1.00 44.58	7
	ATOM	2563	CA	SER			33.797	29.527	30.416	1.00 42.97	6
	ATOM	2564	CB	SER			34.867	28.605	30.935	1.00 42.63	6
	ATOM	2565	OG	SER			34.810	28.586	32.342	1.00 46.80	8
15	MOTA	2566	С	SER	В	116	34.124	30.939	30.832	1.00 43.61	6
	MOTA	2567	0	SER	В	116	35.144	31.473	30.431	1.00 45.91	8
	ATOM	2568	N	ILE			33.270	31.547	31.643	1.00 42.76	7
	MOTA	2569	CA	ILE			33.483	32.923	32.052	1.00 40.88	6
00	MOTA	2570	CB	ILE			32.340	33.816	31.515	1.00 39.30	6
20	MOTA	2571	CG2				32.512	35.249	31.995	1.00 40.17	6
	ATOM	2572	CG1	ILE			32.317	33.760	29.992	1.00 37.44 1.00 36.96	6 6
	MOTA	2573	CD1 C	ILE			31.069 33.592	34.332 33.158	29.394 33.545	1.00 36.96	6
	ATOM ATOM	2574 2575	0	ILE			32.840	32.585	34.329	1.00 42.01	8
25	ATOM	2576	N	ARG			34.554	33.986	33.939	1.00 42.44	7
	ATOM	2577	CA	ARG			34.683	34.363	35.339	1.00 42.12	6
	ATOM	2578	CB	ARG			36.120	34,283	35.835	1.00 39.55	6
	ATOM	2579	CG	ARG			36.241	34.873	37,226	1.00 40.13	` 6
	ATOM	2580	CD	ARG	В	118	37.520	34.517	37.933	1.00 40.72	6
30	ATOM	2581	NE	ARG	В	118	37.546	35.120	39.259	1.00 43.73	7
	MOTA	2582	CZ	ARG			38.424	34.821	40.204	1.00 43.99	6
	MOTA	2583		ARG			39.356	33.915	39.973	1.00 45.99	7
	MOTA	2584	NH2	ARG			38.367	35.427	41.376	1.00 44.09	7
05	MOTA	2585	C	ARG			34.215	35.819	35.332	1.00 42.68	6
35	MOTA	2586	0	ARG			34.657	36.604 36.190	34.503 36.239	1.00 43.76 1.00 41.50	8 7
•	ATOM	2587 2588	N CA	GLN GLN			33.324 32.815	37.553	36.229	1.00 41.30	6
	MOTA MOTA	2589	CB	GLN			31.817	37.664	35.080	1.00 40.73	6
	ATOM	2590	CG	GLN			31.199	39.002	34.850	1.00 37.63	6
40	ATOM	2591	CD	GLN			30.414	39.031	33.553	1.00 38.05	6
	ATOM	2592		GLN			29.835	38.028	33.137	1.00 40.82	8
	MOTA	2593		GLN			30.380	40.181	32.914	1.00 38.24	7
	ATOM	2594	С			119	32.171	37.897	37.561	1.00 41.65	6
	MOTA	2595	0	GLN	В	119	31.660	37.028	38,245	1.00 43.20	8
45	MOTA	2596	N			120	32.208	39.163	37.945	1.00 43.19	7
	MOTA	2597	CA			120	31.606	39.561	39.209	1.00 46.59	6
	MOTA	2598	CB			120	32.500	40.540	39.955	1.00 48.44	6
	ATOM	2599	CG			120	33.874	40.005	40.232	1.00 57.79	6
50	ATOM	2600	CD			120	34.423	40.632	41.493	1.00 64.95 1.00 67.80	6
50	ATOM	2601 2602	NE CZ			120 120	33.964 33.571	39.971 40.624	42.727 43.818	1.00 67.80	7 6
	ATOM ATOM	2602		ARG			33.565	41.958	43.827	1.00 66.34	7
	ATOM	2604		ARG			33.219	39.944	44.913	1.00 69.34	7
	ATOM	2605	C			120	30.241	40.184	38.999	1.00 45.42	6
55	MOTA	2606	ō			120	29.991	40.825	37.979	1.00 43.82	8
	ATOM	2607	N	PHE	В	121	29.361	39.983	39.972	1.00 45.27	7
	ATOM	2608	CA	PHE	В	121	28.012	40.515	39.882	1.00 46.73	6
	ATOM	2609	CB			121	26.998	39.411	39.558	1.00 44.66	6
~~	ATOM	2610	CG			121	27.320	38.639	38.324	1.00 41.56	6
60	MOTA	2611		PHE			28.265	37.621	38.355	1.00 38.98	6
	MOTA	2612	CD2	PHE	В	121	26.698	38.942	37.123	1.00 40.65	6

	WO 01/5	8951								PCT	/EP01/01	1457
							-115					
	λ.π·ΩM	2613	CE1	PHE	20	121	28.585	36.920	37.212	1 00	38.44	6
	ATOM ATOM	2614		PHE			27.013	38.245	35.977	1.00		6
	ATOM	2615	CZ	PHE			27.959	37.232	36.020		37.80	6
	ATOM	2616	C	PHE			27.549	41.193	41.142		47.76	6
5	ATOM	2617	o	PHE			28.094	40.972	42.224		45.87	8
•	ATOM	2618	N .	SER			26.521	42.021	40.966		49.39	7
	ATOM	2619	CA	SER			25,881	42.735	42.054		51.30	6
	MOTA	2620	CB	SER			25.677	44.200	41.680		50.63	6
	ATOM	2621	OG	SER			25.026	44.887	42.726		52.75	8
10	ATOM	2622	C	SER			24.530	42.041	42.235		52.14	6
	ATOM	2623	Õ	SER			23.659	42.135	41.377	1.00	51.12	8
	ATOM	2624	N	CYS			24.371	41.323	43.340		53.84	7
	ATOM	2625	CA	CYS			23.133	40.605	43.603		56.99	6
	ATOM	2626	С	CYS			22.973	40.343	45.111	1.00	58.94	6
15	ATOM	2627	0	CYS	В	123	23.837	40.727	45.911	1.00	58.00	8
	MOTA	2628	СВ	CYS	В	123	23.135	39.282	42.830	1.00	55.83	6
	MOTA	2629	SG	CYS	В	123	24.561	38.231	43.250	1.00	57.55	16
	ATOM	2630	N	ASP			21.874	39.687	45.491		59.24	7
	MOTA	2631	CA	ASP			21.619	39.412	46.893		59.17	6
20	ATOM	2632	CB	ASP			20.148	39.085	47.114		61.47	6
	ATOM	2633	CG	ASP			19.670	39.487	48.505		62.03	6
	ATOM	2634		ASP			20.462	39.403	49.470		60.72	8
	ATOM	2635		ASP			18.493	39.886	48.628		63.80	8
0.5	ATOM	2636	С	ASP			22.470	38.274	47.434		59.25	6
25	ATOM	2637	0	ASP			22.309	37.122	47.036		58.84	8
	MOTA	2638	N	VAL			23.365	38.612	48.356		59.36	7
	ATOM	2639	CA	VAL			24.260	37.647	48.979		59.62	6
•	MOTA	2640	CB	VAL			25.683	38.230	49.080		57.35 54.50	6 6
30	MOTA	2641		VAL			26.599	37.280	49.798		58.35	6
30	ATOM	2642 2643	CGZ	VAL VAL			26.212 23.766	38.519 37.277	47.702 50.378		62.42	6
	ATOM ATOM	2644	0	VAL			24.161	36.254	50.378		64.51	8
	ATOM	2645	N	SER			22.892	38.105	50.939		63.61	7
	ATOM	2646	CA	SER			22.375	37.857	52.283		64.32	6
35	ATOM	2647	CB	SER			21.260	38.857	52.613		63.21	6
-	ATOM	2648	OG	SER			20.175	38.715	51.715		59.22	8
	ATOM	2649	C	SER			21.858	36.429	52.444		64.47	6
	ATOM	2650	0	SER			21.082	35.940	51.626		63.31	8
	ATOM	2651	N	GLY			22.313	35.764	53.496	1.00	65.55	7
40	MOTA	2652	CA	GLY	В	127	21.872	34.409	53.748	1.00	68.84	6
	ATOM	2653	С	GLY	В	127	22.847	33.351	53.282	1.00	70.32	6
	MOTA	2654	0	GLY	В	127	22.634	32.161	.53,500		71.17	8
	MOTA	2655	N	VAL	В	128	23.923	33.776	52.638		71.67	7
	ATOM	2656	CA	VAL	В	128	24.910	32.826	52.148		72.95	6
45	MOTA	2657	CB	VAL			26.107	33.522	51.467		71.97	6
	ATOM	2658		VAL			25.686	34.081	50.149		73.72	6
	ATOM	2659		VAL			26.654	34.614	52.359		69.90	6
	ATOM	2660	C	VAL			25.504	31.942	53.212		73.83	6
E0	ATOM	2661	0	VAL			25.628	30.743	53.016		73.27	8
50	ATOM	2662	N	ASP			25.884	32.542	54.332		75.83	7
	MOTA	2663	CA	ASP			26.532	31.789	55.384 56.504		78.34 79.36	6
	ATOM	2664	CB	ASP			27.008	32.715			81.22	6
	ATOM ATOM	2665 2666	CG OD1	ASP ASP			28.209 29.166	32.141 32.909	57.257 57.523		81.78	6 8
55		2667		ASP			28.202	30.922	57.576		81.70	8
55	ATOM ATOM	2668	C	ASP			25.720	30.548	55.972		80.31	6
	MOTA	2669	0			129	26.293	29.783	56.660		81.06	8
	ATOM	2670	N			130	24.412	30.603	55.706		80.80	7
	MOTA	2671	CA			130	23.640	29.501	56.259		81.78	6
60	ATOM	2672	CB			130	23.681	29.563	57.799		85.11	6
-	MOTA	2673	OG1				24.158	30.862	58.195		84.93	8

	WO 01/58	8951							PCT/EP01/01	457
						-116				
	MOTA	2674	CG2	THR 1	в 130	24.582	28.416	58.388	1.00 85.83	6
	ATOM	2675	С		в 130	22.182	29.286	55.881	1.00 80.84	6
	MOTA	2676	0	THR 1	B 130	21.460	30.224	55.506	1.00 78.93	8
	ATOM	2677	N	GLU 3	в 131	21.784	28.014	56.028	1.00 80.92	7
5	MOTA	2678	CA	GLU I	в 131	20.416	27.510	55.832	1.00 80.70	6
	MOTA	2679	CB	GLU :	в 131	19.435	28.339	56.689	1.00 83.05	6
	MOTA	2680	CG		в 131	19.467	28.017	58.187	1.00 84.49	6
	MOTA	2681	CD		в 131	19.024	29.189	59.051	1.00 85.34	6
	MOTA	2682			B 131	17.948	29.773	58.762	1.00 86.44	8
10	MOTA	2683	OE2		В 131	19.757	29.521	60.019	1.00 85.14	8
	ATOM	2684	C		В 131	19.864	27.420	54.426	1.00 79.07	6
	ATOM	2685	0		B 131	20.207	26.520	53.643	1.00 76.96	8
	ATOM	2686	N		B 132	18.941	28.338	54.156	1.00 78.17	7
1 =	ATOM	2687	CA		B 132	18.298	28.449	52.858	1.00 77.92 1.00 77.07	6 6
15	MOTA	2688	CB		B 132 B 132	16.953 17.130	29.195 30.486	53.001 53.575	1.00 77.45	8
	ATOM ATOM	2689 2690	OG C		B 132	19.277	29.220	51.945	1.00 76.88	6
	ATOM	2691	0		B 132	19.000	29.463	50.759	1.00 77.41	8
	ATOM	2692	_		B 133	20.424	29.588	52.520	1.00 74.38	7
20	ATOM	2693	CA		B 133	21.442	30.308	51.782	1.00 72.04	6
	ATOM	2694	C		B 133	20.943	31.569	51.105	1.00 71.42	6
	ATOM	2695	Ō		в 133	19.888	32.104	51.450	1.00 71.39	8
	ATOM	2696	N		в 134	21.708	32.044	50.125	1.00 69.68	7
	ATOM	2697	CA	ALA	B 134	21.345	33.251	49.390	1.00 66.69	6
25	MOTA	2698	CB	A:LA	в 134	22.534	34.194	49.315	1.00 66.34	6
	MOTA	2699	С		B 134	20.874	32.908	47.993	1.00 64.53	6
	ATOM	2700	0		B 134	21.095	31.802	47.504	1.00 64.56	8
	MOTA	2701	N		B 135	20.207	33.865	47.369	1.00 62.63	7
00	MOTA	2702	CA		B 135	19.719	33.696	46.017	1.00 62.23	6
30	MOTA	2703	CB		B 135	18.205	33.577	45.980	1.00 62.17	6
	ATOM	2704			B 135	17.812	32.456	46.775	1.00 64.85 1.00 62.33	8 6
	ATOM	2705			B 135 B 135	17.721 20.159	33.370 34.900	44.543 45.194	1.00 62.33	6
	ATOM ATOM	2706 2707	C O		B 135	19.618	36.009	45.308	1.00 62.56	8
35	ATOM	2707	N		B 136	21.174	34,661	44.379	1.00 61.14	7
00	ATOM	2709	CA		B 136	21.754	35.668	43.526	1.00 58.61	6
	ATOM	2710	C		B 136	21.159	35.497	42.134	1.00 56.85	6
	ATOM	2711	ō.		B 136	21.308	34.452	41.503	1.00 55.78	8
	ATOM	2712	СВ	CYS	в 136	23.276	35.474	43.527	1.00 58.82	6
40	ATOM	2713	SG		в 136	24.201	36.455	42.315	1.00 60.36	16
	ATOM	2714	N	ARG	в 137	20.453	36.519	41.670	1.00 55.98	7
	MOTA	2715	CA	ARG	в 137	19.845	36.457	40.353	1.00 56.14	6
	MOTA	2716	СВ		B 137	18.421	37.009	40.383	1.00 57.73	6
4=	MOTA	2717	CG		В 137	17.502	36.250	41.303	1.00 62.21	6
45	ATOM	2718	CD		B 137	16.367	37.136	41.792	1.00 68.77	6
	MOTA	2719	NE		B 137	15.827	36.666	43.071	1.00 74.27	7 6
•	MOTA	2720	CZ		B 137	15.070 14.739	35.575 34.822	43.224 42.174	1.00 76.32 1.00 77.05	7
	ATOM ATOM	2721 2722			B 137 B 137		35.221	44.434	1.00 77.03	7
50	ATOM	2723	C		B 137	20.672	37.253	39.366	1.00 55.38	6
00	ATOM	2724	0		в 137	21.052	38.389	39.637	1.00 57.67	8
	MOTA	2725	N		B 138	20.933	36.646	38.215	1.00 52.27	7
	ATOM	2726	CA		B 138		37.255	37.163	1.00 48.96	6
	ATOM	2727	CB		B 138		36.411	36.890	1.00 45.32	6
55	ATOM	2728			в 138	`	37.007	35.749	1.00 42.82	6
	MOTA	2729	CG1		B 138		36.309	38.160	1.00 42.90	6
	MOTA	2730	CD1		B 138		35.313	38.067	1.00 40.32	6
	MOTA	2731	C		B 138		37.313	35.900	1.00 48.66	6
00	MOTA	2732	0		В 138		36.286	35.406	1.00 49.73	8
60	ATOM	2733	N		B 139		38.506	35.375	1.00.48.12	7
	MOTA	2734	CA	ь¥S	в 139	19.822	38.642	34.165	1.00 51.18	6

	WO 01/58951									PCT/E	P01/014	157
							-117					
	АТОМ	2735	СВ	T.VC	_	139	18.775	39.759	34.326	1.00 5	2 02	6
	ATOM	2736	CG	LYS			17.908	39.625	35.553	1.00 5		6
	ATOM	2737	CD	LYS			16.721	40.567	35.523	1.00 5		6
	ATOM	2738	CE	LYS			15.716	40.155	34.461	1.00 5		6
5	ATOM	2739	NZ	LYS			14.539	41.062	34.435	1.00 5		7
•	ATOM	2740	C	LYS			20.686	38.966	32.957	1.00 5		6
	ATOM	2741	ō	LYS			21.461	39.919	32.998	1.00 5		8
	ATOM	2742	N			140	20.561	38.192	31.883	1.00 4		7
	ATOM	2743	CA			140	21.348	38.480	30.696	1.00 4		6
10	MOTA	2744	СВ			140	22.590	37.531	30.607	1.00 4		6
	ATOM	2745		ILE			23.254	37.411	31.973	1.00 5		6
	ATOM	2746		ILE			22.192	36.126	30.217	1.00 5		6
	ATOM	2747	CD1				23.312	35.115	30.483	1.00 5		6
	ATOM	2748	С			140	20.520	38.444	29.410	1.00 4		6
15	ATOM	2749	0			140	19.727	37.545	29.211	1.00 4		8
	MOTA	2750	N	GLY	В	141	20.685	39.448	28.557	1.00 4		7
	MOTA	2751	CA	GLY	В	141	19.941	39.500	27.313	1.00 4	7.33	6
	ATOM	2752	С	GLY	В	141	20.631	40.387	26.293	1.00 4	6.71	6
	ATOM	2753	0	GLY	В	141	21.623	41.025	26.625	1.00 4	7.72	8
20	MOTA	2754	N	SER	В	142	. 20.131	40.425	25.05.8	1.00 4	5.43	7
	MOTA	2755	CA	SER			20.739	41.267	24.026	1.00 4	4.63	6
	MOTA	2756	CB	SER			19.990	41.165	22.706	1.00 4	2.45	6
	ATOM	2757	OG			142	20.431	42.168	21.814	1.00 4	0.68	8
05	ATOM	2758	С	SER			20.774	42.728	24.457	1.00 4		6
25	ATOM	2759	0			142	19.812	43.256	25.031	1.00 4		8
	ATOM	2760	N	TRP			21.888	43.384	24.162	1.00 4		7
	ATOM	2761	CA	TRP			22.069	44.761	24.549	1.00 4		6
	ATOM	2762	CB	TRP			23.553	45.044	24.758	1.00 4		6
30	ATOM	2763	CG	TRP			23.816	46.368	25.388	1.00 4		6
30	ATOM	2764		TRP			23.642	46.697	26.762	1.00 4		6
	ATOM	2765	·CE2	TRP			23.999	48.055	26.920	1.00 4		6
	ATOM ATOM	27,66 27,67	CE3	TRP TRP			23.221	45.975	27.880	1.00 3		6
	ATOM	2768		TRP			24.262 24.373	47.517	24.773	1.00 4		6
35	ATOM	2769		TRP			23.947	48.534 48.694	25.691 28.149	1.00 4		7
-	ATOM	2770		TRP			23.171	46.612	29.097	1.00 3 1.00 3		6 6
	ATOM	2771	CH2	TRP			23.531	47.956	29.224	1.00 3		6
	ATOM	2772	C	TRP			21.499	45.730	23.545	1.00 4		6
	ATOM	2773	ō	TRP			21.062	46.813	23.909	1.00 4		8
40	ATOM	2774	N	THR			21.477	45.358	22.277	1.00 4		7.
	ATOM	2775	CA	THR			20.963	46.287	21.290	1.00 4		6
	MOTA	2776	СВ	THR			22.072	46.696	20.328	1.00 4		6
	ATOM	2777		THR			22.669	45.524	19.763	1.00 4		8
	ATOM	2778		THR			23.129	47.487	21.069	1.00 4		6
45	MOTA	2779	С	THR	В	144	19.778	45.793	20.485	1.00 4	8.06	6
	ATOM	2780	0	THR	В	144	19.136	46.576	19.783	1.00 5	0.29	8
	MOTA	2781	N	HIS	В	145	19.474	44.504	20.584	1.00 4	7.78	7
	MOTA	2782	CA	HIS			18.364	43.970	19.820	1.00 4	8.99	6
	MOTA	2783	CB	HIS			18.800	42.716	19.055	1.00 4	7.81	6
50	MOTA	2784	CG	HIS			19.805	42.974	17.974	1.00 4	6.09	6
	MOTA	2785		HIS			19.677	43.532	16.748	1.00 4		6
	MOTA	2786		HIS			21.125	42.602	18.086	1.00 4		7
	ATOM	2787		HIS			21.766	42.915	16.975	1.00 4		6
55	ATOM	2788		HIS			20.909	43.481	16.146	1.00 4		7
JJ	MOTA	2789	C	HIS			17.149	43.656	20.682	1.00 5		6
	ATOM	2790	0	HIS			17.235	42.933	21.668	1.00 5		8
	ATOM ATOM	2791 2792	N	HIS			16.010	44.213	20.302	1.00 5		7
	ATOM	2792	CA CB	HIS HIS			14.774 13.797	43.974	21.027	1.00 5		6
60	ATOM	2794	CG	HIS			13.797 13.526	45.130 45.413	20.800 19.360	1.00 5		6 6
	ATOM	2795		HIS			13.106	44.605	18.357	1.00 5		6
					_				,,		- • = 3	-

	WO 01/5	8951								PCT	/ <b>EP01</b> /01	1457
							-118					
	ATOM	2796	NTO1	HIS	В	146	13.726	46.653	18.795	1.00	53.68	7
	ATOM	2797		HIS		146	13.448	46.597	17.504		55.84	6
	ATOM	2798		HIS			13.070	45.364	17.212		55.30	7
	ATOM	2799		HIS			14.149	42.647	20.576	1.00	57.05	6
5	ATOM	2800	0	HIS	В	146	14.640	41.984	19.644		58.04	8
	ATOM	2801	N	SER	В	147	13.057	42.280	21.243		58.47	7
	MOTA	2802	CA	SER			12.328	41.037	20.997		58.52	6
	ATOM	2803	СВ	SER			11.071	41.021	21.861		58.93	6
40	ATOM	2804	OG	SER			10.386	42.252	21.740		63.53	8
10	MOTA	2805	С	SER			11.955	40.708	19.557		57.13	6 8
	ATOM	2806	0	SER			11.776	39.545 <b>41</b> .716	19.215 18.709		56.86 56.50	7
	ATOM ATOM	2807 2808	N CA	ARG ARG			11.841 11.473	41.462	17.323		58.81	6
	ATOM	2809	CB	ARG			10.905	42.734	16.691		62.56	6
15	ATOM	2810	CG	ARG			9.781	43.380	17.493		70.38	6
. •	ATOM	2811	CD	ARG			9.337	44.731	16.897		76.49	6
	ATOM	2812	NΕ	ARG			8.480	45.487	17.819		82.57	7
	ATOM	2813	CZ	ARG	в	148	7.263	45.104	18.222	1.00	84.74	б
	ATOM	2814		ARG			6.728	43.965	17.791	1.00	85.52	7
20	ATOM	2815	NH2	ARG			6.573	45.864	19.064	1.00	85.55	7
	ATOM	2816	С	ARG	В	148	12.655	40.963	16.490	1.00	57.83	. 6
	ATOM	2817	0	ARG	В	148	12.474	40.423	15.395		58.23	8
	MOTA	2818	N	GLU			13.864	41.147	17.011		56.99	7
	MOTA	2819	CA	GLU			15.072	40.743	16.306		53.60	6
25	MOTA	2820	CB	GLU			16.015	41.933	16.216		52.91	6
	MOTA	2821	CG	GLU			15.280	43.243	15.955		51.82	6
	ATOM	2822	CD	GLU			16.208	44.437	15.841		54.76 55.52	6 8
	ATOM	2823 2824		GLU GLU			17.132 16.010	44.562 45.261	16.672 14.929		52.75	8
30	ATOM ATOM	2825	OE2 C	GLU			15.729	39.584	17.036		52.78	6
30	MOTA	2825	0	GLU			16.150	38.606	16.421		51.81	8
	ATOM	2827	N	ILE			15.811	39.693	18.355		51.32	7
	ATOM	2828	CA	ILE			16.382	38.619	19.154		51.11	6
	ATOM	2829	CB	ILE			17.770	38.989	19.757		48.77	6
35	АТОМ	2830	CG2				18.155	37.995	20.843	1.00	43.40	6
	ATOM	2831	CG1	ILE	В	150	18.842	38.967	18.672		47.30	6
	MOTA	2832	CD1	ILE	В	150	20.219	39.315	19.168		45.12	6
	ATOM	2833	С	ILE	В	150	15.453	38.254	20.297		53.02	6
	ATOM	2834	0	ILE			14.842	39.116	20.932		52.00	8
40	ATOM	2835	N	SER			15.350	36.955	20.539		55.16	7
	ATOM	2836	CA			151	14.542	36.436	21.628		56.52	. 6
	ATOM	2837	СВ			151	13.280	35.733	21.089		57.06	6
	ATOM	2838	OG			151	13.594	34.585	20.323		54.91 56.69	8 6
45	ATOM	2839	C			151 151	15.452 16.144	35.447	21.685		57.55	8
40	ATOM ATOM	2840 2841	O N	VAL			15.480	35.504	23.661		58.35	7
	ATOM	2842	CA	VAL			16.306	34.600	24.456		60.89	6
	ATOM	2843	CB			152	17.135	35.362	25.502		60.77	6
	ATOM	2844		VAL			17.890	36.489	24.844		59.09	6
50	ATOM	2845	CG2	VAL	В	152	16.220	35.903	26.586	1.00	62.75	6
	ATOM	2846	С	VAL	В	152	15.389	33.632	25.194	1.00	62.80	6
	ATOM	2847	0	VAL	В	152	14.287	34.012	25.597		63.08	8
	MOTA	2848	N			153	15.845	32.395	25.387		64.20	7
	ATOM	2849	CA			153	15.028	31.390	26.061		66.36	6
55	ATOM	2850	CB			153	14.232	30.611	25.016		67.03	6
	ATOM	2851	CG			153	13.427	31.518	24.095		68.33	6
	ATOM	2852		ASP			12.327	31.949	24.504		65.39 70.09	8
	MOTA	2853		ASP			13.905	31.810	22.969 26.872		68.77	8 6
60	MOTA MOTA	285 <u>4</u> 2855	C '	ASP		153	15.877 16.974	30.416 30.049	26.872		69.28	8
	ATOM	2856	N			154	15.404	30.017	28.067		70.46	7
	7.7. O.1.1	2030			_						<b></b>	•

	WO 01/58	951							PCT/EP01/014	57
						-119				
	MOTA	2857	CD		B 154		30.740	28.876	1.00 69.92	6
	MOTA MOTA	2858 2859	CA CB		В 154 В 154		29.070 29.108	28.898 30.225	1.00 72.29	6 6
	ATOM	2860	CG		в 154 В 154		30.494	30.223	1.00 70.76	6
5	ATOM	2861	C		B 154	16.151	27.668	28.250	1.00 05.28	6
•	ATOM	2862	Ö		B 154		27.467	27.187	1.00 75.41	. 8
	ATOM	2863	N		B 155		26.700	28.888	1.00 79.33	7
	ATOM	2864	CA		B 155	16.887	25.350	28.332	1.00 83,13	6
	ATOM	2865	CB		B 155		25.187	27.542	1.00 82.37	6
10	ATOM	2866	OG1	THR	в 155	19.316	25.233	28.453	1.00 83.94	8
	ATOM	2867	CG2		B 155		26.311	26.545	1.00 81.49	6
	ATOM	2868	С		B 155		24.189	29.348	1.00 86.65	6
	ATOM	2869	0		B 155		24.298	30.385	1.00 87.45	8
4-	ATOM	2870	N		B 156		23.078	29.013	1.00 90.57	7
15	ATOM	2871	CA		B 156	17.504	21.839	29.813	1.00 93.48	6
	MOTA	2872	CB		B 156		21.025	29.491	1.00 93.70	6
	ATOM	2873 2874	OG1		В 156 В 156		20.761 19.694	28.077	1.00 92.52	8
	MOTA MOTA	2875			B 156		22.012	30.301 31.337	1.00 93.12 1.00 95.82	6
20	ATOM	2876	С 0		B 156		22.012	31.990	1.00 95.82	6 8
20	ATOM	2877	N		B 157		21.809	31.897	1.00 98.15	7
	ATOM	2878	CA	-	B 157		21.946	33.337	1.00100.26	6
	ATOM	2879	СВ		B 157		22.308	33.606	1.00102.01	6
	ATOM	2880	CG		B 157		23.363	32.643	1.00104.88	6
25	ATOM	2881	CD		B 157		23.649	32.902	1.00106.35	6
	ATOM	2882	OE1	GLU	B 157	11.745	22.665	32.965	1.00106.79	8
	ATOM	2883	OE2	GLU	B 157	12.178	24.850	33.030	1.00105.97	8
	MOTA	2884	C	GLU	B 157	16.397	20.662	34.102	1.00100.31	6
	MOTA	2885	0		B 157		20.631	35.348	1.00100.47	8
30	MOTA	2886	N		B 158		19.601	33.364	1.00 99.66	7
	ATOM	2887	CA		B 158		18.329	34.003	1.00 99.04	6
	MOTA	2888	CB		B 158		17.198	32.969	1.00100.65	6
	MOTA	2889	CG		B 158		17.113	32.170	1.00101.63	6
35	ATOM ATOM	2890 2891			B 158 B 158		16.919 17.254	32.733 30.847	1.00101.77 1.00102.28	8 7
00	MOTA	2892	C		B 158		18.424	34.672	1.00102.28	6
	ATOM	2893	ō		B 158		18.748	35.872	1.00 97.45	8
	MOTA	2894	N		B 159		18.120	33.881	1.00 94.36	7
	ATOM	2895	CA		B 159		18.156	34.300	1.00 90.64	6
40	ATOM	2896	CB		B 159		19.051	33.325	1.00 91.05	6
	ATOM	2897	OG	SER	B 159	20.831	20.167	32.948	1.00 91.42	8
	MOTA	2898	С		B 159		18.622	35.742	1.00 87.58	6
	MOTA	2899	0		B 159		19.741	36.114	1.00 87.04	8
4 =	MOTA	2900	N		B 160		17.767	36.553	1.00 84.29	7
45		2901	CA		B 160		18.137	37.938	1.00 80.73	6
	MOTA	2902	CB		B 160		17.149	38.582	1.00 79.96	6
	ATOM	2903	CG		B 160		17.566	39.991	1.00 79.90	6
	ATOM ATOM	2904 2905			В 160 В 160		17.087 18.362	40.471 40.617	1.00 79.39 1.00 79.13	8 8
50	ATOM	2906	C		B 160		19.514	37.956	1.00 79.13	6
00	ATOM	2907	Ö		B 160		19.687	37.394	1.00 78.08	8
	ATOM	2908	N		B 161		20.473	38.612	1.00 76.06	7
	MOTA	2909	CA		B 161		21.851	38.706	1.00 71.50	6
	ATOM	2910	СВ		в 161		22.683	39.675	1.00 70.10	6
55	MOTA	2911	CG		в 161		22,977	39.130	1.00 69.41	6
	MOTA	2912			в 161		23.189	37.905	1.00 68.26	8
	MOTA	2913			B 161		23.007	39.929	1.00 71.44	8
	MOTA	2914	С		B 161		21.979	39.110	1.00 69.84	6
60	ATOM	2915	0		B 161		23.008	38.843	1.00 71.09	8
60	MOTA	2916	N		B 162		20.960	39.740	1.00 67.23	7
	MOTA	2917	CA	ひ正式	B 162	25.928	21.078	40.136	1.00 67.27	6

		•				-120				
	ATOM	2918	СВ	SER I	3 162	26.051	21.210	41.661	1.00 67.18	6
	ATOM	2919	OG	SER I			20.020	42.315	1.00 66.16	8
	ATOM (	2920	C	SER I			19.922	39.653	1.00 66.71	6
	ATOM	2921	Ō	SER I			19.576	40.289	1.00 64.25	8
5	MOTA	2922	N	GLU I			19.330	38.523	1.00 67.10	7
	ATOM	2923	CA	GLU I	3 16	3 27.192	18.220	38.005	1.00 68.36	6
	ATOM	2924	СВ	GLU I	3 16	3 26.378	17.421	36.970	1.00 70.98	6
	ATOM	2925	CG	GLU I			17.926	35.545	1.00 72.60	6
	ATOM	2926	CD	GLU I	3 16	3 25.726	16.946	34.594	1.00 74.62	6
10	ATOM	2927	OE1	GLU I	3 16	3 24.477	16.828	34.649	1.00 76.45	- 8
	MOTA	2928	OE2	GLU I	3 16	3 26.428	16.285	33.798	1.00 74.37	8
	ATOM	2929	С	GLU I	3 16	3 28.530	18.688	37.410	1.00 67.51	6
	MOTA	2930	0	GLU I			17.868	37.070	1.00 67.13	8
	MOTA	2931	N	TYR I			20.008	37.294	1.00 66.57	7
15	MOTA	2932	CA	TYR I			20.583	36.771	1.00 64.39	6
	MOTA	2933	CB	TYR I			21.419	35.526	1.00 64.28	6
	ATOM	2934	CG	TYR 1			20.602	34.354	1.00 66.44	6
	MOTA	2935		TYR I			20.860	33.766	1.00 66.70	6
	MOTA	2936	CE1	TYR I			20.105	32.690	1.00 66.59	6
20	ATOM	2937	CD2				19.556	33.832	1.00 65.02	6
	ATOM	2938	CE2	TYR I			18.790	32.756	1.00 65.71	6
	ATOM	2939	CZ	TYR I			19.075	32.184	1.00 66.77 1.00 67.83	6
	ATOM ATOM	2940 2941	OH	TYR I			18.369 21.463	31.084 37.826	1.00 67.83	8 6
25	ATOM	2941	C 0	TYR			21.403	37.662	1.00 61.67	8
20	MOTA	2942	N	PHE :			21.673	38.918	1.00 61.88	7
	ATOM	2944	CA	PHE I		•	22.517	39.990	1.00 60.70	6
	ATOM	2945	CB	PHE I			22.704	41.067	1.00 58.78	6
	ATOM	2946	CG	PHE			23.905	41.941	1.00 57.08	6
30	ATOM	2947		PHE :			25.184	41.413	1.00 56.05	6
	MOTA	2948	CD2	PHE 1	B 16	5 29.888	23.757	43.272	1.00 54.09	6
	MOTA	2949	CE1	PHE 1	3 16	5 29.680	26.296	42.200	1.00 55.95	6
	MOTA	2950	CE2	PHE :			24.858	44.063	1.00 55.48	6
	MOTA	2951	CZ	PHE :			26,131	43.530	1.00 56.15	6
35	MOTA	2952	C	PHE 1			21.960	40.614	1.00 59.91	6
	ATOM	2953	0	PHE			20.760	40.808	1.00 60.17	8
•	ATOM	2954	N	SER I			22.839	40.919	1.00 60.28	7
	ATOM	2955	CA	SER I			22.390	41.532	1.00 60.24 1.00 59.33	6
40	MOTA	2956	CB	SER SER			23.534 23.081	41.647 42.239	1.00 59.33	6 8
40	MOTA ATOM	2957 2958	OG C	SER :			21.877	42.239	1.00 59.12	6
	ATOM	2959	0	SER :			22.434	43.611	1.00 60.02	8
	MOTA	2960	N	GLN :			20.815	43.319	1.00 61.73	7
	ATOM	2961	CA	GLN :			20.228	44.623	1.00 62.29	6
45	ATOM	2962	CB	GLN			18.737	44.576	1.00 63.96	6
	MOTA	2963	CG	GLN :			18.442	44.068	1.00 66.77	6
	MOTA	2964	CD	GLN :			16.969	43.736	1.00 68.16	6
	ATOM	2965	OE1	GLN :	в 16		16.103	44.605	1.00 66.24	8
	ATOM	2966	NE2	GLN :	в 16	7 36.136	16.682	42.465	1.00 68.10	7
50	MOTA	2967	С	GLN			20.912	45.689	1.00 60.72	6
	MOTA	2968	0	GLN			20.814	46.880	1.00 62.24	8
	ATOM	2969	N	TYR			21.626	45.269	1.00 57.81	7
	ATOM	2970	CA	TYR			22.291	46.235	1.00 56.47	6
55	MOTA	2971	CB	TYR			22.236	45.741	1.00 55.55	6
55	ATOM	2972	CG CD1	TYR			20.836	45.330	1.00 55.77	6
	ATOM ATOM	2973 2974		TYR TYR			20.447 19.139	43.988 43.617	1.00 53.38 1.00 53.39	6 6
	ATOM	2974	CD2				19.139	46.286	1.00 55.39	6
	ATOM	2976		TYR			18.561	45.922	1.00 54.41	6
60	ATOM	2977	CZ	TYR			18.207	44.591	1.00 54.89	6
	ATOM	2978	OH	TYR.			16.919	44.227	1.00 56.81	8

WO 01/58951	•	,	PCT/EP01/01457

						-121				_
	MOTA	2979		TYR I		36.222	23.712	46.586	1.00 55.31	6
	MOTA	2980	0	TYR I		36.891	24.395	47.356	1.00 54.88	8
	MOTA	2981	N	SER I		35.097	24.140	46.033	1.00 55.16	7
_	MOTA	2982	CA	SER E		34.570	25.469	46.299	1.00 57.04	6
5	MOTA	2983	CB	SER I		33.363	25.755	45.412	1.00 55.22	6
	MOTA	2984	OG	SER I	3 169	32.775	26.991	45.769	1.00 55.21	8
	MOTA	2985	С	SER I	3 169	34.147	25.617	47.754	1.00 60.21	6
	ATOM	2986	0	SER I	3 169	33.664	24.671	48.380	1.00 62.02	8
	MOTA	2987	N	ARG 1	3 170	34.321	26.815	48.298	1.00 61.79	7
10	ATOM	2988	CA	ARG 1		33.938	27.059	49.678	1.00 60.59	6
	MOTA	2989	CB	ARG 1	в 170	34.467	28.417	50.150	1.00 61.26	6
	ATOM	2990	CG	ARG 1	3 170	35.781	28.342	50.904	1.00 61.61	6
	MOTA	2991	CD	ARG :	в 170	36.588	29.628	50.764	1.00 66.75	6
	MOTA	2992	NE	ARG 1	в 170	35.866	30.846	51.158	1.00 69.32	7
15	ATOM	2993	CZ	ARG :	в 170	35.634	31.877	50.342	1.00 68.59	6
	MOTA	2994	NH1	ARG :	B 170	36.053	31.840	49.079	1.00 65.59	7
	MOTA	2995	NH2	ARG :	в 170	35.017	32.959	50.803	1.00 69.04	7
	ATOM	2996	Ċ	ARG :	в 170	32.431	27.041	49.785	1.00 58.91	6
	MOTA	2997	0	ARG :	B 170	31.892	26.981	50.883	1.00 61.10	8
20	MOTA	2998	N	PHE :	B 171	31.748	27.077	48.650	1.00 56.02	7
	ATOM	2999	CA	PHE	B 171	30.294	27.093	48.674	1.00 56.85	6
	ATOM	3000	CB	PHE	B 171	29.782	28.384	48.033	1.00 56.79	6
	MOTA	3001	CG	PHE	B 171	30.498	29.608	48.529	1.00 59.30	6
	ATOM	3002			B 171	31.806	29.889	48.110	1.00 59.59	б
25	MOTA	3003	CD2	PHE	в 171	29.900	30.447	49.462	1.00 58.28	6
	MOTA	3004	CE1	PHE	B 171	32.497	30.983	48.616	1.00 58.87	6
	MOTA	3005	CE2	PHE	B 171	30.586	31.546	49.978	1.00 57.19	6
	MOTA	3006	CZ	PHE	в 171	31.883	31.817	49.556	1.00 58.74	6
	ATOM	3007	С		B 171	29.694	25.892	47.987	1.00 57.50	6
30	ATOM	3008	0		B 171	30.412	25.063	47.439	1.00 57.83	8
	MOTA	3009	N		B 172		25.793	48.036	1.00 58.25	7
	MOTA	3010	CA		B 172	27.671	24.681	47.416	1.00 58.95	6
	MOTA	3011	CB		в 172	27.418	23.555	48.436	1.00 61.94	6
	MOTA	3012	·CG		В 172	26.521	23.921	49.634	1.00 65.83	6
35	ATOM	3013	CD		B 172	26.352	22.769	50.637	1.00 67.36	6
	MOTA	3014		•	B 172	26.275	21.593	50.192	1.00 67.12	8
	ATOM	3015	OE2		B 172	26.280	23.043	51.868	1.00 67.97	8
	ATOM	3016	С		В 172	26.369	25.197	46.844	1.00 59.12	6
	ATOM	3017	0		В 172		26.217	47.302	1.00 58.48	8
40	ATOM	3018	N		B 173	25.865	24.502	45.831	1.00 59.47	7
	MOTA	3019	CA		в 173	24.630	24.911	45.180	1.00 60.85	6
	MOTA	3020	CB		B 173	24.715	24.729	43.653	1.00 62.04	6
	MOTA	3021			В 173	23.369	25.077	42.998	1.00 60.25	6
4 =	ATOM	3022			В 173	25.832	25.603	43.087	1.00 62.02	6
45	ATOM	3023			B 173	26.018	25.413	41.600	1.00 63.88	6
	ATOM	3024	С		B 173	23.415	24.148	45.667	1.00 61.72	6
	MOTA	3025	0		В 173	23.415	22.919	45.733	1.00 61.55	8
	MOTA	3026	N		В 174	22.369		45.999	1.00 62.91	7
<b>-</b> 0	ATOM	3027	CA		B 174	21.158	24.253	46.460	1.00 63.63	6
50	MOTA	3028	CB		B 174	20.438	25.166	47.443	1.00 63.66	6
	ATOM	3029	CG		B 174	21.339	25.698	48.556	1.00 64.21 1.00 63.13	6
	ATOM	3030			B 174		26.678	49.428		6
	ATOM	3031			B 174		24.532	49.369	1.00 61.09 1.00 64.20	6
	ATOM	3032	C .		B 174		24.010	45.232		6
55	ATOM	3033	0		B 174		22.885	44.962	1.00 65.99	8
	ATOM	3034	N		B 175		25.058	44.459	1.00 64.89 1.00 66.77	7
	ATOM	3035	CA		B 175		24.895	43.268 43.691	1.00 68.40	6
	MOTA	3036	CB		B 175		24.785		1.00 70.08	6 6
80	ATOM	3037	CG OD1		B 175		24.566	42.508 41.695	1.00 70.08	8
60	MOTA	3038			B 175		23.631 25.322	42.404	1.00 71.36	8
	MOTA	3039	200	MOL	B .175	13.003	۵۵،۵۵۵	46.404	2.00 07.30	o

PCT/EP01/01457

WO 01/58951

	WO 01/5	0931							PC 1/EF	J1/U143	′
						-122					
	ATOM	3040	С	ASP E	175	19.480	26.067	42.298	1.00 67.	12	6
	ATOM	3040	0	ASP I		19.910	27.160	42.703	1.00 67.		8
	MOTA	3042	N	VAL I		19.214	25.818	41.018	1.00 66.		7
	MOTA	3043	CA	VAL I		19.364	26.819	39.981	1.00 65.		6
5	ATOM	3044	СВ	VAL I		20.616	26.547	39.112	1.00 64.		6
_	ATOM	3045		VAL I		20.681	27.529	37.943	1.00 62.		6
	ATOM	3046		VAL E		21.866	26.645	39.964	1.00 64.		6
	ATOM	3047	С	VAL E		18.139	26.760	39.088	1.00 66.		6
	ATOM	3048	0	VAL I	3 176	17.723	25.682	38.657	1.00 68.	14	8
10	MOTA	3049	N	THR I	3 177	17.555	27.920	38.816	1.00 68.		7
	MOTA	3050	CA	THR I		16.393	27.988	37.939	1.00 70.		6
	ATOM	3051	CB	THR I		15.087	28.139	38.744	1.00 69.		б
	MOTA	3052		THR I		15.203	29.253	39.638	1.00 70.		8
4-	ATOM	3053	CG2	THR I		14.821	26.885	39.544	1.00 68.		6
15	MOTA	3054	C	THR I		16.537	29.173	36.984	1.00 72.		6
	ATOM	3055	0	THR I		17.095	30.220	37.356	1.00.74.		8
	ATOM	3056	N	GLN I		16.049	29.002	35.757	1.00 73. 1.00 74.		7 6
	ATOM ATOM	3057 3058	CA CB	GLN I		16.121 17.006	30.057 29.619	34.756 33.594	1.00 74.		6
20	ATOM	3059	CG	GLN I		18.090	28.628	33.984	1.00 70		6
	ATOM	3060	CD	GLN 1		19.227	28.575	32.959	1.00 83		6
	ATOM	3061		GLN I		18.993	28.495	31.731	1.00 83		8
	ATOM	3062	NE2			20.469	28.616	33.458	1.00 82		7
	ATOM	3063	С	GLN I		14.725	30.354	34.232	1.00 73		6
25	MOTA	3064	0	GLN 1	3 178	14.041	29.454	33.752	1.00 75	.30	8
	MOTA	3065	N	LYS 1	3 179	14.306	31.611	34.310	1.00 73		7
	MOTA	3066	CA	LYS 1		12.978	31.995	33.837	1.00 72		6
	ATOM	3067	CB	LYS 1		12.076	32.307	35.030	1.00 75		6
00	ATOM	3068	CG	LYS I		12.196	31.282	36.160	1.00 78		6
30	ATOM	3069	CD	LYS I		11.456	31.735	37.428	1.00 80		6
	MOTA	3070 3071	CE NZ	LYS I		11.845 13.320	30.874 30.987	38.631 38.927	1.00 80		6 7
	ATOM ATOM	3071	C	LYS		13.320	33.232	32.961	1.00 70		6
	ATOM	3072	ο.		3 179	13.411	34.311	33.455	1.00 70		8
35	ATOM	3074	N	LYS		12.852	33.090	31.665	1.00 68		7
	ATOM	3075	CA		3 180	12.970	34.242	30.776	1.00 68		6
	ATOM	3076	CB	LYS :	3 180	12.873	33.792	29.305	1.00 66	.36	6
	ATOM	3077	CG	LYS I	3 180	11.517	33.383	28.831	1.00 61	. 57	6
	ATOM	3078	CD	LYS 1	3 180	10.763	34.578	28.296	1.00 62		6
40	ATOM	3079	CE		3 180	11.419	35.168	27.058	1.00 63		6
	ATOM	3080	ŊΖ		3 180	11.317	34.295	25.857	1.00 64		7
	ATOM	3081	C	LYS I		11.914	35.297	31.096	1.00 69		6
	MOTA	3082	0		B 180	11.131	35.112	32.019 30.366	1.00 70		8 7
45	MOTA	3083 3084	N		8 181 8 181	11.922 10.927	36.416 37.473	30.560	1.00 69 1.00 70		6
40	ATOM ATOM	3085	CA CB		3 181	10.755	37.816	32.052	1.00 70		6
	ATOM	3086	CG		B 181	12.058	38.021	32.760	1.00 71		6
	ATOM	3087		ASN		12.935	38.731	32.267	1.00 71		8
	ATOM	3088		ASN :		12.195	37.412	33.940	1.00 71		7
50	ATOM	3089	С	ASN 3	B 181	11.125	38.768	29.779	1.00 70	. 25	6
	ATOM	3090	0	ASN :	B 181	12.104	39.478	29.975	1.00 70		8
	MOTA	3091	N		B 182	10.162	39.078	28.911	1.00 70		7
	MOTA	3092	CA		B 182	10.203	40.297	28.105	1.00 70		6
E E	MOTA	3093	CB		B 182	9.107	40.262	27.045	1.00 70		6
55	MOTA	3094	OG		B 182	9.267	41.327	26.122	1.00 71		8.
	ATOM ATOM	3095 3096	С О		B 182 B 182	9.997 9.429	41.500 41.359	29.024 30.095	1.00 70 1.00 72		6 8
	ATOM	3096	N		B 183	10.442	42.680	28.600	1.00 72		7
	MOTA	3098	CA		B 183	10.334	43.887	29.425	1.00 70		6
60	ATOM	3099	CB		B 183	11.337	43.826	30.630	1.00 68		6
	MOTA	3100	CG1	VAL		12.636	43.178	30.202	1.00 68		6

PCT/EP01/01457

WO 01/58951

MOTA

ATOM

MOTA

MOTA

MOTA

60

-123 3101 CG2 VAL B 183 11.625 45.230 31.148 MOTA 1.00 67.78 6 VAL B 183 10.590 45.189 28.659 1.00 70.59 MOTA 3102 C 6 45.282 27.853 MOTA 3103 VAL B 183 11.522 1.00 71.25 8 0 46.195 28.911 9.761 MOTA 3104 N THR B 184 1.00 70.21 7 9.949 5 THR B 184 47.480 28.250 1.00 71.59 ATOM 3105 CA 6 8.610 48.062 27.711 1.00 70.78 6 3106 THR B 184 ATOM CB OG1 THR B 184 8.065 47.183 26.721 1.00 69.37 ATOM 3107 8 CG2 THR B 184 8.836 49.431 27.074 ATOM 3108 1.00 69.81 6 THR B 184 3109 10.558 48.447 29.271 1.00 73.13 ATOM С 6 10 ATOM 3110 THR B 184 10.240 48.384 30.467 1.00 73.23 0 MOTA 3111 TYR B 185 11.449 49.319 28.806 1:00 74.37 N ATOM 3112 TYR B 185 12.085 50.287 29.689 1.00 76.17 CA ATOM 3113 TYR B 185 13.614 50.134 29.663 1.00 77.19 б CB MOTA 3114 CG TYR B 185 14.076 48.723 29.912 1.00 78.36 6 15 ATOM 3115 CD1 TYR B 185 13.942 47.745 28.928 1.00 78.94 6 MOTA 3116 14.298 46.417 ·29.178 1.00 80.41 CE1 TYR B 185 б 14.584 48.344 31.154 MOTA 3117 CD2 TYR B 185 1.00 79.09 6 MOTA 3118 CE2 TYR B 185 14.944 47.013 31.413 1.00 79.41 6 46.054 30.424 44.731 30.677 51.670 29.209 MOTA TYR B 185 14.796 1.00 79.27 3119 CZ6 20 MOTA 3120 TYR B 185 15.119 1.00 79.15 OH 8 11.713 1.00 76.81 MOTA 3121 С TYR B 185 6 51.927 28.003 **TYR B 185** 1.00 76.75 ATOM 3122 0 11.669 8 52.563 30.152 11.445 1.00 78.68 ATOM 3123 N SER B 186 7 11.078 53.941 29.810 1.00 80.19
11.002 54.795 31.089 1.00 80.19
12.160 54.610 31.902 1.00 79.86
12.100 54.539 28.832 1.00 80.21
11.745 55.296 27.923 1.00 79.15
13.364 54.171 29.025 1.00 80.45
14.459 54.653 28.189 1.00 80.85
14.259 54.260 26.772 1.00 81.01
14.510 55.018 25.838 1.00 80.34
15.787 53.993 28.574 1.00 81.53
15.913 52.165 28.268 1.00 84.25
13.791 53.035 26.637 1.00 82.80
13.712 52.411 25.339 1.00 83.26
12.352 51.851 24.849 1.00 82.46 11.078 53.941 29.810 1.00 80.00 CA SER B 186 MOTA 3124 6 25 CB SER B 186 ATOM 3125 6 ATOM 3126 OG SER B 186 8 SER B 186 MOTA 3127 С ATOM 3128 0 SER B 186 MOTA 3129 N CYS B 187 30 MOTA 3130 CA CYS B 187 6 MOTA CYS B 187 3131 C 6 MOTA CYS B 187 3132 0 8 MOTA 3133 CB CYS B 187 6 ATOM 3134 CYS B 187 SG 16 35 MOTA 3135 N CYS B 188 7 MOTA CYS B 188 3136 CA 6 MOTA 3137 CYS B 188 C CYS B 188 MOTA 3138 0 8 14.811 51.336 25.365 1.00 82.41 CYS B 188 MOTA 3139 CB 6 40 ATOM 3140 CYS B 188 16.353 51.824 26.282 1.00 83.49 SG 16 ATOM 3141 PRO B 189 11.891 52.346 23.679 1.00 81.48 N 7 12.734 53.291 22.910 ATOM 3142 CD PRO B 189 1.00 81.13 6 PRO B 189 10.652 52.037 22.938 1.00 79.97 MOTA 3143 CA 6 **ATOM** 3144 PRO B 189 10.977 52.510 21.517 1.00 80.12 CB 6 10.977 52.510 21.517 1.00 80.12 11.825 53.725 21.766 1.00 80.41 10.133 50.585 22.941 1.00 78.77 9.063 50.303 23.490 1.00 78.66 10.878 49.671 22.313 1.00 77.68 10.473 48.254 22.219 1.00 73.96 11.214 47.570 21.075 1.00 75.24 11.578 48.475 19.908 1.00 77.67 10.414 48.680 18.950 1.00 79.11 9.731 47.672 18.617 1.00 77.05 10.200 49.845 18.526 1.00 79.84 45 ATOM 3145 CG PRO B 189 PRO B 189 MOTA 3146 С PRO B 189 MOTA 3147 0 8 GLU B 190 ATOM 3148 N 7 ATOM 3149 CA GLU B 190 б 50 GLU B 190 ATOM 3150 CB 6 ATOM 3151 GLU B 190 CG 6 MOTA 3152 CD GLU B 190 MOTA OE1 GLU B 190 3153 8 3154 OE2 GLU B 190 10.200 49.845 18.526 1.00 79.84 ATOM 8 10.23 55 C GLU B 190 1.00 71.49 MOTA 3155 47.482 23.494 6 3155 C GLU B 190 3156 O GLU B 190 3157 N ALA B 191 3158 CA ALA B 191 3159 CB ALA B 191 3160 C ALA B 191 3161 O ALA B 191 11.317 48.038 24.460 ATOM 1.00 71.14

10.455 46.191 23.483

10.708 45.331 24.638

44.340 24.801

44.570 24.489

12.439 44.225 23.374 1.00 63.36

9.554

12.035

1.00 68.33

1.00 66.03

1.00 65.95

1.00 64.66

7

	WO 01/58	8951							PCT/EP01/01	457
						-124		•		
	ATOM	3162	Ν.	TYR I	3 192			25.608	1.00 62.75	7
	ATOM	3163	CA	TYR					1.00 61.63	6
	MOTA	3164	CB	TYR I			34 44.468	26.010	1.00 59.80	6
_	MOTA	3165	CG	TYR :					1.00 59.56	6
5	ATOM	3166		TYR :					1.00 59.46	6
	ATOM	3167		TYR :					1.00 60.27	6
	MOTA	3168		TYR :					1.00 60.64 1.00 60.97	6 6
	ATOM ATOM	3169 3170	CE2 CZ	TYR :					1.00 61.60	6
10	ATOM	3171	OH	TYR :					1.00 60.81	8
. •	ATOM	3172	C	TYR					1.00 62.58	6
	ATOM	3173	Ō	TYR :					1.00 62.03	8
	ATOM	3174	N	GLU :	B 193	13.8	34 41.166	25.738	1.00 62.66	7
	ATOM	3175	CA	GLU :					1.00 62.77	6
15	MOTA	3176	CB		B 193				1.00 61.29	6
	MOTA	3177	CG	GLU :					1.00 61.98	6
	MOTA	3178	CD	GLU :					1.00 62.41 1.00 62.14	6 8
	ATOM ATOM	3179 3180		GLU :					1.00 62.14	8
20	ATOM	3181	C		B 193				1.00 61.37	6
	ATOM	3182	ō	GLU					1.00 63.09	8
	ATOM	3183	N	ASP					1.00 58.46	7
	ATOM	3184	CA	ASP			07 38.395	28.914	1.00 57.68	6
	ATOM	3185	CB	ASP					1.00 58.80	6
25	MOTA	3186	CG	ASP					1.00 61.20	6
	ATOM	3187		ASP					1.00 63.41	8
	MOTA	3188	-	ASP					1.00 59.40	8
	MOTA MOTA	3189 3190	C		B 194 B 194				1.00 56.01 1.00 55.53	6 8
30	ATOM	3191	O N	VAL					1.00 55.28	7
00	ATOM	3192	CA	VAL					1.00 54.79	6
	ATOM	3193		VAL					1.00 53.86	6
	ATOM	3194	CG1	VAL	в 195				1.00 51.98	6
	ATOM	3195	CG2	VAL	в 195	17.1	12 33.631	28.968	1.00 53.24	6
35	ATOM	3196	С		B 195				1.00 56.42	6
	ATOM	3197	0		B 195				1.00 58.47	8
	ATOM	3198	N		B 196				1.00 58.06	7
	ATOM .	3199 3200	CA CB		B 196 B 196				1.00 58.06 1.00 59.44	6 6
40	ATOM	3200	CG		B 196				1.00 64.02	6
70	ATOM	3202	CD		B 196				1.00 65.27	6
	ATOM	3203		GLU					1.00 65.41	8
	MOTA	3204		GLU					1.00 68.06	8
	MOTA	3205	C		B 196				1.00 57.73	6
45	ATOM	3206	0		B 196				1.00 60.64	8
	MOTA	3207	Ŋ		B 197				1.00 56.14	7
	MOTA	3208	CA		B 19'				1.00 54.69 1.00 52.53	6 6
	ATOM ATOM	3209 3210	CB CC1	VAL	B 191				1.00 52.55	6
50	ATOM	3211		VAL					1.00 51.73	6
	ATOM	3212	C		в 19'				1.00 56.80	6
	ATOM	3213	0		в 19				1.00 57.91	8
	ATOM	3214	N	SER	B 19	3 .18.5	39 32.258	38.631	1.00 58.59	7
	ATOM	3215	CA		B 19				1.00 58.65	6
55	ATOM	3216	CB		B 19				1.00 59.34	6
	ATOM	3217	OG		B 19				1.00 59.29	8
	ATOM	3218	C		B 198				1.00 57.58 1.00 58.41	6 8
	ATOM ATOM	3219 3220	N O		B 19				1.00 57.49	7
60	ATOM	3221	CA		B 19				1.00 58.89	6
	ATOM	3222	CB		B 19			7 41.622	1.00 58.76	6

	WO 01/5	8951							PCT/EP01/01	457
						-125				
	ATOM	3223	CG	LEU E	3 199	24.108	30.670	42.358	1.00 59.80	6
	MOTA	3224		LEU I		24.135	29.209	41.927	1.00 60.58	6
	ATOM	3225		LEU I		25.446	31.304	42.063	1.00 60.42	6
	ATOM	3226	C		3 199	21.369	30.885	43.395	1.00 60.51	6
5	MOTA	3227	0		3 199	21.759	31.788	44.136	1.00 61.67	8
	ATOM	3228	N.	ASN I	B 200	20.754	29.801	43.838	1.00 60.15	7
	ATOM	3229	CA	ASN I	B 200	20.539	29.607	45.252	1.00 57.57	6
	ATOM	3230	CB		B 200	19.188	28.919	45.499	1.00 60.95	6
	MOTA	3231	CG		В 200	18.936	28.642	46.968	1.00 62.80	6
10	MOTA	3232			в 200	19.167	29.504	47.820	1.00 65.10	8
	MOTA	3233	ND2		B 200	18.465	27.443	47.275	1.00 59.90	7
	MOTA	3234	C		B 200	21.691		45,712	1.00 55.80	6
	ATOM	3235	0		B 200	21.793	27.569	45.325	1.00 56.54	8 7
1 =	ATOM	3236	N		B 201	22.561	29.316 28.615	46.527 47.042	1.00 53.98 1.00 53.98	6
15	MOTA	3237	CA		B 201 B 201	23.725 24.960	28.975	46.226	1.00 53.35	6
	ATOM ATOM	3238 3239	CB CG		B 201	25.418	30.404	46.418	1.00 51.26	6
	ATOM	3239			B 201	26.633	30.690	47.050	1.00 50.15	6
	ATOM	3241			B 201	24.615	31.472	46.000	1.00 50.67	6
20	ATOM	3242			B 201	27.038	32.015	47.264	1.00 45.58	6
	ATOM	3243	CE2		B 201	25.016	32.799	46.213	1.00 47.69	6
	ATOM	3244	CZ	PHE	B 201	26.227	33.062	46.845	1.00 46.26	6
	ATOM	3245	С	PHE	B 201	23.943	29.080	48.456	1.00 55.95	6
	MOTA	3246	0	PHE	B 201	23.275	30.017	48.912	1.00 56.39	8
25	ATOM	3247	N		B 202	24.896	28.443	49.132	1.00 56.81	7
	MOTA	3248	CA		B 202	25.223	28.793	50.506	1.00 60.77	6
	MOTA	3249	CB		B 202	24.255	28.104	51.460	1.00 64.25	. 6
	ATOM	3250	CG		B 202	24.491	26.625	51.497	1.00 66.78 1.00 70.08	6 6
20	ATOM	3251	CD		B 202	23.494	25.893 24.454	52.344 52.333	1.00 70.08	7
30	ATOM	3252 3253	NE CZ		B 202 B 202	23.768 22.945	23.528	52.825	1.00 72.03	6
	ATOM ATOM	3254			B 202	21.781	23.884	53.375	1.00 74.01	7
	ATOM	3255			B 202	23.281	22.245	52.760	1.00 73.29	7
	ATOM	3256	C		B 202	26.635	28.328	50.843	1.00 61.67	6
35	ATOM	3257	ō		B 202	27.181	27.450	50.183	1.00 62.10	8
	ATOM	3258	N		B 203	27.225	28.918	51.875	1.00 62.58	7
	ATOM	3259	CA	LYS	B 203	28.549	28.505	52.298	1.00 62.87	6
	ATOM	3260	CB	LYS	B 203	29.067	29.417	53.399	1.00 62.83	6
	ATOM	3261	CG		B 203	30.400	28.995	53.967	1.00 62.29	6
40	MOTA	3262	CD		B 203	30.765	29.871	55.141	1.00 65.39	6
	ATOM	3263	CE		В 203		29.519	55.689	1.00 67.38	6
	MOTA	3264	NZ		B 203		29.772	54.695	1.00 70.43 1.00 64.30	7 6
	ATOM	3265	C		B 203		27.101 26.736	52.854 53.371	1.00 65.43	8
45	MOTA	3266 3267	O N		B 203		26.736	52.745	1.00 66.12	7
40	ATOM ATOM	3268	N CA		B 204		24.955	53.246	1.00 67.10	6
	MOTA	3269	CB		B 204		24.223	52.860	1.00 63.37	6
	ATOM	3270	CG		B 204		23.853	51.379	1.00 60.21	6
	ATOM	3271	CD		B 204		22.966	51.055	1.00 58.61	6
50	ATOM	3272	CE		B 204		22.553	49.582	1.00 57.79	6
	MOTA	3273	NZ	LYS	B 204	33.202	21.808	49.238	1.00 53.82	7
	ATOM	3274	С		B 204		25.081	54.745	1.00 70.90	6
	MOTA	3275	0		B 204		25.989	55.339	1.00 72.60	8
	ATOM	3276	N		B 205		24.192	55.342	1.00 74.01	7
55	ATOM	3277	CA		B 205		24.197	56.783	1.00 74.37	6
	MOTA	3278	C		B 205		23.430	57.576	1.00 75.59 1.00 75.56	6 8
	MOTA	3279			B 205		22.932 23.331	56.958 58.822	1.00 75.36	8
	ATOM	3280 3281	CB	PHE	B 205		48.183	2.177	1.00 70.47	6
60	ATOM ATOM	3281	CB	PHE			49.162	1.297	1.00 73.66	6
-	ATOM	3283		PHE			48.805	0.647	1.00 74.99	6
	•									

	WO 01/5	8951					•			PCT/EP01/0	1457
							-126				
	ATOM	3284	CD2	PHE	C	1	16.889	50.471	1.160	1.00 75.46	6
	ATOM	3285		PHE		1	19.257	49.743	-0.138	1.00 77.68	6
	ATOM	3286		PHE		1	17.590	51.421	0.380	1.00 76.94	6
	ATOM	3287	CZ	PHE		1	18.779	51.054	-0.271	1.00 77.37	6
5	ATOM	3288	С	PHE		1	16.469	45.841	2.896	1.00 69.30	6
	MOTA	3289	0	PHE		1	15.487	45.976	3.637	1.00 68.12	8
	MOTA	3290	N	PHE		1	15.624	46.515	0.608	1.00 67.59	7
	ATOM	3291	CA	PHE		1	16.651	46.733	1.669	1.00 69.36	6 7
10	ATOM ATOM	3292 3293	N CA	ASP ASP		2 2	17.421 17.373	44.940 44.071	3.123 4.298	1.00 69.61 1.00 68.32	6
10	MOTA	3294	CB	ASP		2	17.364	42.592	3.882	1.00 69.98	6
	ATOM	3295	CG	ASP		2	18.729	42.092	3.426	1.00 71.56	6
	ATOM	3296	OD1	ASP		2	19.586	41.867	4.316	1.00 71.73	8
	ATOM	3297	OD2	ASP		2	18.936	41.926	2.187	1.00 72.36	8
15	ATOM	3298	С	ASP		2	18.615	44.399	5.116	1.00 66.00	6
	ATOM	3299	0	ASP		2	19.617	44.865	4.562	1.00 67.56	8
	MOTA	3300	N.	ARG		3	18.550	44.165	6.423 7.320	1.00 62.29	. 7
	ATOM ATOM	3301 3302	CA CB	ARG ARG		3 3	19.663 19.515	44.455 43.661	8.604	1.00 59.37 1.00 56.89	6 6
20	ATOM	3302	CG	ARG		3	18.280	44.017	9.387	1.00 55.35	6
	ATOM	3304	CD	ARG		3	18.177	43.172	10.640	1.00 57.70	6
	ATOM	3305	NE	ARG		3	16.947	43.437	11.378	1.00 60.36	7
	ATOM	3306	CZ	ARG		3	16.714	44.540	12.084	1.00 62.92	6
~~	ATOM	3307		ARG		3	17.623	45.503	12.166	1.00 62.53	7
25	MOTA	3308		ARG		3	15.554	44.689	12.700	1.00 64.87	7
	ATOM	3309	C	ARG		3	21.060	44.236	6.749	1.00 59.30	6
	ATOM ATOM	3310 3311	N N	ARG ALA		3 4	21.970 21.257	45.008 43.215	7.051 5.920	1.00 61.36 1.00 57.54	8 7
	ATOM	3311	CA	ALA		4	22.595	43.023	5.379	1.00 55.37	6
30	ATOM	3313	СВ	ALA		4	22.686	41.727	4.610	1.00 53.55	6
	ATOM	3314	С	ALA	С	4	22.947	44.186	4.478	1.00 54.97	6
	MOTA	3315	0	ALA		4	24.020	44.764	4.603	1.00 55.12	8
	MOTA	3316	N	ASP		5	22.034	44.534	3.575	1.00 56.24	7
35	ATOM	3317	CA	ASP		5	22.265	45.632	2.646	1.00 56.25	6
33	ATOM ATOM	3318 3319	CB CG	ASP ASP		5 5	21.081 20.773	45.795 44.529	1.680 0.906	1.00 58.72 1.00 62.35	6 6
	ATOM	3320		ASP		5	21.715	43.900	0.364	1.00 63.21	8
	ATOM	3321		ASP		5	19.574	44.171	0.834	1.00 65.38	8
	ATOM	3322	С	ASP		5	22.471	46.935	3.406	1.00 55.27	6
40	MOTA	3323	0	ASP	С	5	23.294	47.764	3.020	1.00 54.31	8
	ATOM	3324	N	ILE		6	21.732	47.110	4.495	1.00 53.55	7
	ATOM	3325	CA	ILE		6	21.840	48.339	5.270	1.00 54.16	6
	ATOM ATOM	3326 3327	CB	ILE		6 6	20.713 20:811	48.456 49.793	6.311 7.021	1.00 54.45 1.00 52.65	6 6
45	ATOM	3328		ILE		6	19.352	48.344	5.612	1.00 56.53	6
	ATOM	3329		ILE		6	18.146	48.530	6.524	1.00 56.74	6
	ATOM	3330	C	ILE		6	23.178	48.475	5.972	1.00 52.95	6
	ATOM	3331	0	ILE	C	6	23.872	49.487	5.818	1.00 53.74	8
	ATOM	3332	N	LEU		7	23.543	47.455	6.741	1.00 51.30	7
50	ATOM	3333	CA	LEU		7	24.814	47.462	7.460	1.00 49.62	6
	ATOM	3334	CB	LEU		7	24.931 23.912	46.194 46.136	8.293 9.429	1.00 47.45 1.00 47.62	6
	ATOM ATOM	3335 3336	CG CD1	LEU LEU		7 7	.23.819	44.743	10.014	1.00 47.02	6 6
	ATOM	3337		LEU		7	24.321	47.122	10.486	1.00 47.41	6
55	MOTA	3338	C	LEU		7	25.970	47.559	6.465	1.00 49.71	6
	MOTA	3339	0	LEU	С	7	26.951	48.269	6.677	1.00 47.57	8
	ATOM	3340	N	TYR		8	25.827	46.845	5.361	1.00 52.00	7
	MOTA	3341	CA	TYR		8	26.830	46.838	4.318		6
60	ATOM ATOM	3342 3343	CB CG	TYR TYR		8	26.367 27.335	45.961 45.969	3.167 2.020	1.00 53.82 1.00 57.66	6 6
50	ATOM	3344		TYR		8	28.552	45.289	2.106	1.00 58.72	6

	WO 01/5	8951									PCT	/ <b>EP01</b> /01	457
							-	127	•				
	ATOM	3345	CE1	TYR	С	8		.467	45.315	1.045	1.00	60.33	6
	ATOM	3346	CD2	TYR	С	8		.051	46.679	0.851		58.73	6
	MOTA	3347		TYR		8		.957	46.714	-0.211	_	60.05	6
_	ATOM	3348	CZ	TYR		8		.162	46.027	-0.107		60.68	6
5	ATOM	3349	OH	TYR		8		.045	46.045	-1.163		62.86	8
	MOTA	3350	C	TYR		8		1.134	48.235	3.790		54.25	6
	MOTA	3351	0	TYR		8		298	48.589	3.614		55.00 53.76	8 7
	MOTA	3352	N	ASN ASN		9 9		.092 .283	49.015 50.369	3.516 3.013		55.35	6
10	ATOM ATOM	3353 3354	CA CB	ASN		9	_	.941	51.005	2.660		59.27	6
10	ATOM	3355	CG	ASN		9		1.299	50.372	1.433		61.31	6
	ATOM	3356		ASN		9		907	49.531	0.758		61.18	8
	ATOM	3357		ASN		9		.068	50.778	1.136		62.69	7
	ATOM	3358	С	ASN		9	27	.003	51.233	4.034	1.00	54.14	6
15	MOTA	3359	0	ASN	С	9	28	3.001	51.877	3.722		54.09	8
	MOTA	3360	N	ILE		10		.494	51.240	5.258		54.05	7
	ATOM	3361	CA	ILE		10		7.107	52.014	6.330		54.35	6
	ATOM	3362	CB	ILE		10		399	51.757	7.668	_	53.88	6
20	ATOM	3363		ILE		10		7.141	52.453	8.784		52.27	6
20	ATOM	3364 3365		ILE		10 10		1.956	52.257 51.860	7.595 8.769		53.43 51.08	6 6
	ATOM ATOM	3366	CDI	ILE		10		3.580	51.635	6.479		55.70	6
	ATOM	3367	0	ILE		10		9.452	52.497	6.609		56.88	8
	ATOM	3368	N	ARG		11		3.844	50.337	6.456		56.11	7
25	ATOM	3369	CA	ARG		11		194	49.827	6.579		57.74	6
	ATOM	3370	CB	ARG		11	30	0.161	48.307	6.466	1.00	61.80	6
	ATOM	3371	CG	ARG	С	11	31	L.495	47.629	6.644	1.00	67.28	6
	ATOM	3372	CD	ARG		11		L.879	47.631	8.102		75.61	6
	MOTA	3373	NE	ARG		11		2.848	46.586	8.419		82.91	7
30	ATOM	3374	CZ	ARG		11		2.779	45.333	7.957		86.49	6
	MOTA	3375		ARG		11		L.785	44.963	7.140		87.62	7 7
	MOTA	3376	NH2 C	ARG ARG		11 11		3.689 L.099	44.436 50.388	8.331 5.490		87.96 57.06	6
	MOTA ATOM	3377 3378	0	ARG		11		2.198	50.865	5.758		57.56	8
35	MOTA	3379	N	GLN		12		0.617	50.333	4.255		57.22	7
•	MOTA	3380	CA	GLN		12		1.377	50.781	3.093		56.59	6
	ATOM	3381	СВ	GLN		12		0.783	50.169	1.829		56.62	6
	ATOM	3382	CG	GLN		12		1.795	49.448	0.976	1.00	58.01	6
	MOTA	3383	CD	GLN	С	12		2.113	48.101	1.532		58.10	6
40	MOTA	3384	OE1			12		1.215	47.289	1.704		59.91	8
	MOTA	3385		GLN		12		3.384	47.846	1.824		57.19	7
	MOTA	3386	C	GLN		12		1.505	52.278	2.872		56.02	6
	MOTA	3387	0	GLN		12		2.424	52.728	2.208		54.27 58.04	8 7
45	ATOM ATOM	3388 3389	N CA	THR THR		13 13		0.631	53.054 54.492	3.423 3.213		59.72	6
49	ATOM	3390	CB	THR		13		9.302	54.985	2.653		58.83	6
	ATOM	3391		THR		13		B.253	54.622	3.559		55.46	8
	ATOM	3392		THR		13		9.043	54.374	1.277		59.29	6
	ATOM	3393	С	THR		13		0.944	55.316	4.459	1.00	61.81	6
50	MOTA	3394	0	THR	С	13	33	1.317	56.492	4.364	1.00	62.06	8
	ATOM	3395	N	SER	С	14		0.794	54.705	5.627		62,55	7
	ATOM	3396	CA	SER		14		1.053	55.421	6.865		62.19	6
	MOTA	3397	CB	SER		14		0.549	54.612	8.056		62.76	6
EE	ATOM	3398	OG	SER		14		0.476	55.435	9.209		64.16	8
55	ATOM	3399	C	SER		14		2.521	55.779	7.074 6.577		61.03 61.70	6 8
	MOTA MOTA	3400 3401	N O	SER ARG		14 15		3.422 2.735	55.098 56.863	7.816		58.93	7
	ATOM	3401	CA	ARG		15		4.064	57.367	8.127		57.11	6
	ATOM	3403	СВ	ARG		15		4.383	58.576			57.80	. 6
60	MOTA	3404	CG	ARG		15		4.388	58.261	5.748		59.34	6
	MOTA	3405	CD	ARG		15	. 3.	5.114	59.331	4.968	1.00	61.90	6

	WO 01/5	8951							PCT/EP01/01	457
						-128				
	MOTA	3406	NE	ARG (	C 15	36.475	59.479	5.475	1.00 64.09	7
	MOTA	3407	CZ	ARG (			60.488	5.180	1.00 63.60	6
	MOTA	3408		ARG (			61.450	4.375	1.00 62.16	7
_	ATOM	3409		ARG (			60.526	5.688	1.00 66.26	7
5	ATOM	3410	C	ARG (			57.753	9.598	1.00 54.80	6
	MOTA	3411	0	ARG			58.874	9.969	1.00 54.31	8
	ATOM	3412	N	PRO (			56.811	10.460	1.00 53.16	7 6
	ATOM	3413	CD	PRO (			55.451	10.106 11.911	1.00 49.32 1.00 51.93	6
10	MOTA MOTA	3414 3415	CA CB	PRO (			57.012 55.668	12.429	1.00 49.26	6
10	MOTA	3416	CG	PRO			54.702	11.387	1.00 48.93	6
	ATOM	3417	C	PRO			58.172	12.356	1.00 51.62	6
	ATOM	3418	Ö	PRO			58.663	13.468	1.00 52.27	8
	ATOM	3419	N	ASP			58.608	11.501	1.00 51.78	7
15	MOTA	3420	CA	ASP			59.706	11.863	1.00 54.16	6
	MOTA	3421	CB	ASP		38.597	59.526	11.209	1.00 59.36	6
	MOTA	3422	CG	ASP	C 17	39.421	58.411	11.859	1.00 64.02	6
	MOTA	3423		ASP		39.200	58.134	13.067	1.00 64.61	, 8
	MOTA	3424		ASP (			57.824	11.170	1.00 64.76	8
20	ATOM	3425	C ·	ASP			61.080	11.499	1.00 53.77	6
	ATOM	3426	0	ASP			62.088	11.736	1.00 54.82	8
	ATOM	3427	N	VAL			61.129	10.944	1.00 53.02	7
	MOTA	3428	CA	VAL			62.398	10.528	1.00 53.40	6
25	ATOM	3429	CB	VAL VAL			62.421 63.785	9.003 8.563	1.00 53.89 1.00 53.62	6 6
20	MOTA MOTA	3430 3431		VAL			62.087	8.308	1.00 52.31	6
	ATOM	3432	C	VAL			62.771	11.201	1.00 54.75	6
	ATOM	3433	0	VAL			62.097	11.046	1.00 54.30	8
	ATOM	3434	N	ILE			63.870	11.944	1.00 56.30	7
30	ATOM	3435	CA	ILE			64.401	12.662	1.00 55.34	6
	ATOM	3436	СB	ILE	C 19		65.631	13.519	1.00 54.46	6
	MOTA	3437	CG2	ILE	C 19	33.362	66.777	12.618	1.00 53.28	6
	ATOM	3438	CG1				66.078	14.467	1.00 53.52	6
~=	ATOM	3439		ILE			67.022	15.525	1.00 50.20	6
35	ATOM	3440	С	ILE			64.784	11.644	1.00 56.25	6
	MOTA	3441	0	ILE			65.474	10.653	1.00 56.64	8
	ATOM	3442	N	PRO			64.318	11.861	1.00 55.95 1.00 55.72	7
	ATOM	3443 3444	CD	PRO PRO			63.451 64.574	12.978 10.996	1.00 53.72	6 6
40	ATOM ATOM	3445	CB	PRO			63.627	11.540	1.00 57.07	6
70	ATOM	3446	CG	PRO			62.639	12.349	1.00 57.30	6
	ATOM	3447	C	PRO			66.023	11.035	1.00 59.85	6
	MOTA	3448	Ō	PRO			66.290	11.270	1.00 58.63	8
	ATOM	3449	N	THR		29.416	66.947	10.782	1.00 64.15	7
45	MOTA	3450	CA	THR	C 23	29.123	68.370	10.797	1.00 68.52	6
	MOTA	3451	CB	THR			69.169	11.046	1.00 68.47	6
	ATOM	3452		THR			69.477	12.440	1.00 70.47	8
	MOTA	3453	CG2				70.455	10.216	1.00 69.90	6
50	ATOM	3454	C	THR			68.913	9.555	1.00 72.31 1.00 71.25	6
30	ATOM ATOM	3455 3456	O N	THR GLN			68.631 69.709	8.412 9.805	1.00 71.25	8 7
	ATOM	3457	CA	GLN			70.346	8,747	1.00 70.01	6
	ATOM	3458	CB	GLN			70.087	8.972	1.00 81.49	6
	ATOM	3459	CG	GLN			68.606	9.029	1.00 82.93	6
55	ATOM	3460	CD	GLN			68.351	9.900	1.00 83.25	6
	MOTA	3461		GLN			68.595	11.120	1.00 84.14	8
	ATOM	3462		GLN		22.452	67.867	9.285	1.00 83.14	7
	ATOM	3463	C	GLN			71.846	8.814	1.00 83.04	6
	MOTA	3464	0	GLN			72.523	9.730	1.00 83.36	8
60	ATOM	3465	N	ARG			72.357	7.849	1.00 85.46	7
	MOTA	3466	CA	ARG	C 23	3 27.985	73.783	7.802	1.00 86.39	6

	WO 01/5	8951							,	PCT/EP01/01	457
							-129				
	ATOM	3467	CB	ARG	c :	23	26.722	74.654	7.771	1.00 87.20	6
	MOTA	3468	CG	ARG	c :	23	26.050	74.710	6.393	1.00 89.96	6
	MOTA	3469		ARG		23	24.797	73.834	6.297	1.00 90.96	6
_	MOTA	3470		ARG		23	24.282	73.771	4.920	1.00 93.30	7
5	MOTA	3471	CZ	ARG		23	23.996	74.830	4.145	1.00 94.77	6
	ATOM	3472		ARG		23	24.167	76.083	4.591	1.00 94.25	7
	MOTA	3473		ARG		23	23.537 28.828	74.640	2.905	1.00 94.32 1.00 85.61	7 6
	MOTA	3474		ARG ARG		23 23	29.599	74.134 73.302	9.013 9.495	1.00 85.81	8
10	ATOM ATOM	3475 3476	. O N	ASP		24	28.700	75.358	9.503	1.00 85.83	7
10	ATOM	3477	CA	ASP		24	29.462	75.755	10.685	1.00 86.66	6
	ATOM	3478	CB	ASP		24	29.625	77.283	10.785	1.00 90.61	6
	ATOM	3479	CG	ASP		24	29.385	78.002	9.458	1.00 92.74	6
	ATOM	3480		ASP	C :	24	30.108	77.704	8.471	1.00 93.41	8
15	MOTA	3481	OD2	ASP	C :	24	28.468	78.868	9.418	1.00 93.68	8
	MOTA	3482	С	ASP		24	28.679	75.280	11.907	1.00 85.20	6
	ATOM	3483	0	ASP		24	29.053	75.591	13.052	1.00 85.29	8
	ATOM	3484	N	ARG		25	27.587	74.553	11.660	1.00 82.29	7
00	ATOM	3485	CA	ARG		25	26.761	74.039	12.742	1.00 79.75	. 6
20	MOTA	3486	CB	ARG		25	25.422	73.522	12.210	1.00 82.55 1.00 86.91	6 6
	ATOM	3487	CG	ARG		25 25	24.428 23.026	74.588 73.964	11.781 11.594	1.00 88.91	6
	ATOM ATOM	3488 3489	CD NE	ARG ARG		25 25	22.007	74.963	11.252	1.00 94.97	7
	ATOM	3499	CZ	ARG		25 25	20.702	74.705	11.146	1.00 96.54	6
25	ATOM	3491		ARG		25	20.752	73.471	11.356	1.00 97.65	7
20	ATOM	3492		ARG		25	19.844	75.679	10.837	1.00 96.40	7
	ATOM	3493	C	ARG		25	27.456	72.906	13.490	1.00 76.53	6
	ATOM	3494	ō	ARG		25	28.004	71.987	12.876	1.00 78.25	8
	ATOM	3495	N	PRO	С	26	27.449	72.963	14.829	1.00 72.39	7
30	ATOM	3496	CD	PRO	С	26	27.074	74.126	15.647	1.00 71.70	6
	ATOM	3497	CA	PRO		26	28.073	71.935	15.660	1.00 68.13	6
	ATOM	3498	CB	PRO		26	28.087	72.574	17.050	1.00 69.12	6
	ATOM	3499	CG	PRO		26	28.066	74.039	16.770	1.00 69.98	6
35	ATOM	3500	C	PRO PRO		26 26	27.183 26.010	70.706 70.795	15.639 15.275	1.00 64.71 1.00 63.13	6 8
33	MOTA MOTA	3501 3502	<b>И</b>	VAL		20 27	27.735	69.560	16.019	1.00 61.55	7
	ATOM	3502	CA	VAL		27	26.937	68.349	16.013	1.00 57.92	6
	ATOM	3504	CB	VAL		27	27.805	67.073	15.948	1.00 56.85	6
	ATOM	3505	_	VAL		27	27.038	65.860	16.439	1.00 54.71	6
40	ATOM	3506		VAL		27	28.197	66.872	14.502	1.00 54.24	6
	ATOM	3507	C	VAL		27	26.301	68.400	17.452	1.00 56.84	6
	ATOM	3508	0	VAL	С	27	26.987	68.621	18.450	1.00 57.02	8
	MOTA	3509	N	ALA		28	24.989	68.228	17.506	1.00 56.11	7
	ATOM	3510	CA	ALA		28	24.302	68.262	18.783	1.00 54.82	6
45	ATOM	3511	CB	ALA		28	22.896	68.775	18.600	1.00 55.72	6
	ATOM	3512	C	ALA		28	24.282	66.879	19.424	1.00 54.45	6 8
	ATOM	3513	0	ALA		28 29	23.579 25.067	65.972 66.742	18.964 20.488	1.00 54.53 1.00 53.25	7
	ATOM ATOM	3514 3515	N CA	VAL VAL		29 29	25.191	65.503	21.235	1.00 51.65	6
50	ATOM	3516	CB	VAL		29	26.676	65.113	21.450	1.00 50.25	6
-	ATOM	3517		VAL		29	26.770	63.846	22.297	1.00 47.03	6
	ATOM	3518		VAL		29	27.358	64.921	20.108	1.00 50.21	6
	MOTA	3519	C	VAL		29	24.549	65.670	22.595	1.00 52.02	6
	ATOM	3520	0	VAL		29	24.833	66.615	23.320	1.00 51.40	8
55	ATOM	3521	N	SER		30	23.669	64.745	22.932	1.00 53.81	7
	ATOM	3522	CA	SER		30	23.012	64.785	24.214	1.00 55.39	6
	ATOM	3523	CB	SER		30	21.495	64.666	24.034	1.00 54.53	6
	ATOM	3524	OG	SER		30	21.159	63.462	23.373	1.00 56.88	8
60	ATOM	3525	C	SER		30	23.566	63.614	25.013	1.00 55.69	6
60	ATOM	3526	O N	SER		30	23.688	62.504	24.503 26.261	1.00 56.19 1.00 56.76	8 7
	MOTA	3527	N	VAL	U	31	23.916	63.888	40.201	1.00 30.76	1

	WO 01/5	8951								PCT/EP01/014	57
	•						-130				
	ATOM	3528	CA	VAL	_	31	24.466	62.893	27.174	1.00 57.06	6
	ATOM	3529	CB	VAL		31	25.871	63.301	27.640	1.00 57.34	6
	ATOM	3530		VAL		31	26.543	62.141	28.354	1.00 57.65	6
	АТОМ	3531		VAL		31	26.674	63.784	26.467	1.00 58.89	6
5	ATOM	3532	C	VAL		31	23.585	62.791	28.415	1.00 57.25	6
_	MOTA	3533	ō	VAL		31	23.152	63.806	28.979	1.00 57.25	8
	ATOM	3534	N	SER		32	23.339	61.569	28.855	1.00 56.49	7
	ATOM	3535	CA	SER		32	22.505	61.356	30.024	1.00.57.63	6
	ATOM	3536	СВ	SER	С	32	21.045	61.182	29.589	1.00 59.80	6
10	ATOM	3537	OG	SER	С	32	20.220	60.763	30.667	1.00 63.17	8
	ATOM	3538	С	SER	С	32	22.958	60.123	30.781	1.00 57.81	6
	ATOM	3539	0	SER	С	32	22.860	58.998	30.271	1.00 60.21	8
	MOTA	3540	N	LEU		33	23.448	60.317	31.997	1.00 56.08	7
	ATOM	3541	CA	LEU	С	33	23.895	59.182	32.801	1.00 55.73	6
15	ATOM .	3542	CB	LEU	С	33	25.021	59.581	33.752	1.00 53.14	6
	ATOM	3543	CG	LEU		33	26.240	60.219	33.105	1.00 52.98	6
	MOTA	3544		LEU		33	27.353	60.346	34.127	1.00 51.17	б
	ATOM	3545		LEU		33	26.680	59.374	31.933	1.00 53.34	6
00	ATOM	3546	C	LEU		33	22.752	58.629	33.624	1.00 56.29	6
20	ATOM	3547	0	LEU		33	21.976	59.392	34.193	1.00 57.63	8
	ATOM	3548	N	LYS		34	22.642	57.303	33.664	1.00 54.96	7
	ATOM	3549	CA	LYS		34	21.616	56.643	34.447	1.00 55.26	6
	ATOM	3550	CB	LYS		34	20.710	55.790	33.563	1.00 58.99	6
25	ATOM	3551	CG	LYS		34	20.053	56.544	32.414	1.00 63.56	6
23	ATOM	3552	CD CE	LYS LYS		34 34	19.098 18. <b>4</b> 99	57.649 58.434	32.897	1.00 68.99 1.00 71.13	·6
	ATOM ATOM	3553 3554	NZ	LYS		34	17.528	59.497	31.705 32.120	1.00 71.13	7
	ATOM	3555	C	LYS		34	22.410	55.756	35.369	1.00 71.38	6
	ATOM	3556	0	LYS		34	23.034	54.806	34.922	1.00 54.63	8
30	MOTA	3557	N	PHE		35	22.410	56.064	36.657	1.00 54.05	7
-	ATOM	3558	CA	PHE		35	23.190	55.260	37.579	1.00 51.26	6
	ATOM	3559	CB	PHE		35	23.427	56.032	38.864	1.00 49.55	6
	ATOM	3560	CG	PHE		35	24.291	57.226	38.662	1.00 48.89	6
	ATOM	3561	CD1			35	23.745	58.428	38.239	1.00 48.34	6
35	ATOM	3562		PHE		35	25.669	57.133	38.814	1.00 50.53	6
	ATOM	3563	CE1	PHE	С	35	24.553	59.526	37.967	1.00 47.39	6
	MOTA	3564	CE2	PHE	С	35	26.488	58.228	38.542	1.00 50.75	6
	ATOM	3565	CZ	PHE	С	35	25.925	59.424	38.118	1.00 49.19	6
	ATOM	3566	С	PHE		35	22.608	53.899	37.849	1.00 50.23	6
40	MOTA	3567	0	PHE		35	21.418	53.754	38.078	1.00 50.29	8
	ATOM	3568	N	ILE		36	23.478	52.901	37.795	1.00 49.55	7
	MOTA	3569	CA	ILE		36	23.095	51.519	37.997	1.00 47.28	б
	MOTA	3570	CB	ILE		36	23.658	50.632	36.883	1.00 46.86	6
4 ==	ATOM	3571		ILE		36	23.173	49.223	37.055	1.00 44.45	6
45	ATOM	3572		ILE		36	23.252	51.192	35.521	1.00 46.79	6
	ATOM	3573		ILE		36	21.754	51.310	35.328	1.00 48.67	6
	MOTA	3574	C	ILE		36	23.619	50.999	39.308	1.00 46.88 1.00 48.98	6
	ATOM	3575	0	ILE		36 37	23.052	50.074	39.866	1.00 45.50	8 7
50	MOTA MOTA	3576 3577	N CA	asn asn		37	24.711 25.271	51.578 51.124	39.799 41.061	1.00 44.80	6
00	ATOM	3578	CB	ASN		37	25.738	49.678	40.919	1.00 44.35	6
	ATOM	3579	CG	ASN		37	25.685	48.919	42.226	1.00 44.35	6
	ATOM	3580		ASN		37	26.077	49.424	43.285	1.00 47.36	8
	ATOM	3581		ASN		37	25.209	47.688	42.157	1.00 50.05	7
55	ATOM	3582	C	ASN		37	26.430	51.985	41.573	1.00 44.84	6
	ATOM	3583	Ō	ASN		37	27.089	52.678	40.810	1.00 42.36	8
	MOTA	3584	N	ILE		38	26.654	51.939	42.882	1.00 45.30	7
	ATOM	3585	CA	ILE	С	38	27.735	52,671	43.518	1.00 46.27	6
	ATOM	3586	CB	ILE	C	38	27.186		44.434	1.00 44.46	6
60	MOTA	3587		ILE		38	28.319	54.433	45.178	1.00 42.73	6
	ATOM	3588	CG1	ILE	С	38	26.418	54.770	43.584	1.00 42.70	6

	WO 01/58	8951					-131			PCT	EP01/01	457
	ATOM	3589	CD1	ILE	C	38	25.630	55.758	44.343	1 00	40.81	6
	ATOM	3590	C	ILE		38	28.432	51.585	44.306		49.67	6
	ATOM	3591	ō	ILE		38	27.890	51,083	45.281		53.17	8
	ATOM	3592	N	LEU		39	29.636	51.228	43.872		51.33	7
5	ATOM	3593	CA	LEU		39	30.378	50.125	44.468		53.07	6
	ATOM	3594	CB	LEU		39	31.113	49.384	43.353		53.88	6
	ATOM	3595	CG	LEU	С	39	30.167	49.000	42.215		55.35	6
	ATOM	3596	CD1	LEU	С	39	30.932	48.308	41.115		54.78	6
	ATOM	3597		LEU		39	29.053	48.097	42.760		54.41	6
10	ATOM	3598	С	LEU		39	31.334	50.367	45.619		53.89	6
	ATOM	3599	0	LEU		39	31.386	49.567	46.558		53.73	8
	ATOM	3600	N	GLU		40	32.124	51.426	45.536		54.34	7
	ATOM	3601	CA	GLU		40	33.058	51.714	46.602		56.97	6
15	ATOM	3602	CB	GLU		40	34.446	51.211	46.271		59.79 67.48	6
15	ATOM	3603	CG	GLU		40 40	34.555 35.996	49.711 49.266	46.147 45.979		70.43	6 6
	ATOM ATOM	3604 3605	CD OF1	GLU		40	36.647	49.719	44.998		71.96	8
	ATOM	3606	OE1	GLU		40	36.471	48.476	46.832		71.19	8
	ATOM	3607	C	GLU		40	33.125	53.192	46.823		57.35	6
20	ATOM	3608	ō	GLU		40	33.163	53.975	45.886		58.85	8
	ATOM	3609	N	VAL		41	33.132	53.572	48.084	1.00	57.50	7
	MOTA	3610	CA	VAL	С	41	33.202	54.964	48.440	1.00	56.50	6
	MOTA	3611	CB	VAL	С	41	31.845	55.447	49.000	1.00	57.37	6
	MOTA	3612	CG1	VAL	С	41	31.972	56.832	49.567	1.00	56.32	6
25	MOTA	3613		VAL		41	30.797	55.437	47.894		57.94	6
	MOTA	3614	С	VAL		41	34.289	55.098	49.486		55.27	6
	MOTA	3615	0	VAL		41	34.502	54.200	50.300		54.09	8
	ATOM	3616	N	ASN		42	34.994	56.216	49.433		55.74 56.05	7 6
30	ATOM	3617 3618	CA CB	ASN ASN		42 42	36.053 37.418	56.504 56.169	50.379 49.787		53.93	6
50	ATOM ATOM	3619	CG	ASN		42	38.509	56.155	50.833		53.86	6
	ATOM	3620		ASN		42	38.622	57.075	51.634		54.42	8
	ATOM	3621		ASN		42	39.325	55.110	50.828		54.04	7
	ATOM	3622	C	ASN		42	35.947	57.994	50.635	1.00	58.42	6
35	MOTA	3623	0	ASN	С	42	36.322	58.806	49.786	1.00	58.83	8
	MOTA	3624	N	GLU		43	35.408	58.348	51.801		60.55	7
	ATOM	3625	CA	GLU		43	35.242	59.744	52.163		61.17	6
	MOTA	3626	CB	GLU		43	34.269	59.874	53.327		63.37	6
40	MOTA	3627	CG	GLU		43	33.932	61.318	53.646		67.39	6
40	MOTA	3628	CD	GLU		43	32.773	61.463 62.613	54.616 55.019		68.69 69.27	6 8
	MOTA	3629		GLU		43 43	32.494 32.142	60.444	54.964		68.84	8
	ATOM ATOM	3630 3631	C	GLU GLU		43	36.571	60.391	52.524		60.37	6
	MOTA	3632	Ö	GLU		43	36.706	61.611	52.459		59.71	8
45	ATOM	3633	N	ILE		44	37.544	59.567	52.903		59.67	7
	ATOM	3634	CA	ILE		44	38.874	60.051	53.254	1.00	60.12	6
	ATOM	3635	CB	ILE	С	44	39.727	58.944	53,908		60.72	6
	MOTA	3636	CG2	ILE	С	44	41.124	59.469	54.194		61.61	6
	ATOM	3637		ILE		44	39.081	58.470	55.206		62.18	6
50	ATOM	3638		ILE		44	39.142	59.479	56.325		63.46	6
	MOTA	3639	C	ILE		44	39.617	60.514	51.998		59.74	6
	MOTA	3640	0	ILE		44	40.255 39.540	61.569 59.710	51.988 50.944		60.88 57.16	8 7
	MOTA	3641	N	THR		45	40.221	60.022	49.698		54.13	6
55	ATOM ATOM	3642 3643	CA CB	THR THR		45 45	40.819	58.743	49.056		52.62	6
	MOTA	3644		THR		45	39.776	57.810	48.773		52.62	8
	MOTA	3645		THR		45	41.812	58.106	49.985		52.65	6
	MOTA	3646	C	THR		45	39.325	60.706	48.675	1.00	51.85	6
	MOTA	3647	0	THR		45	39.801	61.196	47.664		51.94	8
60	MOTA	3648	N	ASN		46	38.029	60.736	48.933		51.51	7
	MOTA	3649	CA	ASN	С	46	37.106	61.367	48.002	1.00	52.39	6

	WO 01/5	8951								PCT/E	P01/01	457
							-132					
	ATOM	3650	СВ	ASN (	~	46	37.420	62.856	47.890	1.00 54	4.02	6
	ATOM	3651	CG	ASN (		46	36.525	63.703	48.766	1.00 5		6
	ATOM	3652		ASN		46	36.877	64.821	49.132	1.00 5		8
	ATOM	3653		ASN		46	35.357	63.182	49.093	1.00 5		7
5	ATOM	3654	C	ASN		46	37.143	60.711	46.618	1.00 5	2.56	6
_	ATOM	3655	0	ASN		46	37.269	61.376	45.587	1:00 5	1.60	· 8
	ATOM	3656	N	GLU	C	47	37.013	59.392	46.610	1.00 5		7
	MOTA	3657	CA	GLU		47	37.023	58.633	45.376	1.00 5		6
	MOTA	3658	CB	GLU		47	38.307	57.805	45.300	1.00 4		6
10	MOTA	3659	CG	GLU		47	39.566	58.650	45.210	1.00 4		6
	ATOM	3660	CD	GLU		47	40.823	57.810	45.227	1.00 5		6
	ATOM	3661		GLU		47	40.741	56.621	44.860	1.00 5		8
	ATOM	3662		GLU		47	41.892	58.339	45.595	1.00 5		8
15	ATOM	3663	C	GLU		47	35.793	57.734	45.314	1.00 4		6 8
15	ATOM	3664	0	GLU		47 48	35.403 35.178	57.133 57.654	46.300 44.147	1.00 4		7.
	MOTA	3665 3666	N CA	VAL VAL		48	33.998	56.834	43.993	1.00 4		6
	ATOM ATOM	3667	CB	VAL		48	32.768	57.701	43.736	1.00 5		6
	ATOM	3668		VAL		48	31.549	56.834	43.578	1.00 5		6
20	MOTA	3669		VAL		48	32.567	58.645	44.869	1.00 5		6
	ATOM	3670	C	VAL		48	34.130	55.838	42.850	1.00 4		6
	ATOM	3671	Ō	VAL		48	34.686	56.146	41.802	1.00 4	9.93	8
	ATOM	3672	N	ASP		49	33.615	54.636	43.068	1.00 4	9.86	7
	MOTA	3673	CA	ASP	С	49	33.646	53.595	42.061	1.00 4		6
25	MOTA	3674	CB	ASP	С	49	34.261	52.331	42.644	1.00 5		6
	ATOM	3675	CG	ASP		49	34.714	51.366	41.580	1.00 5		6
	MOTA	3676		ASP		49	33.992	51.233	40.581	1.00 5		8
	MOTA	3677		ASP		49	35.777	50.736	41.748	1.00 5		8
00	MOTA	3678	C	ASP		49	32.181	53.382	41.728	1.00 4		6
30	MOTA	3679	0	ASP		49	31.437	52.818	42.524	1.00 5		8 7
	MOTA	3680	N	VAL		50	31.770 30.374	53.840 53.757	40.551 40.147	1.00 4		6
	MOTA	3681 3682	CA CB	VAL VAL		50 50	29.755	55.185	40.147	1.00 5		, <b>6</b>
	ATOM ATOM	3683		VAL		50	30.212	55.964	38.944	1.00 5		6
35	ATOM	3684		VAL		50	28.248	55.120	40.223	1.00 5		6
-	ATOM	3685	C	VAL		50	30.130	53.122	38.771	1.00 4		6
	ATOM	3686	ō	VAL		50	31.012	53.080	37.928	1.00 4		8
	ATOM	3687	N	VAL		51	28.917	52.621	38.574	1.00 4		7
	ATOM	3688	CA	VAL		51	28.484	52.003	37.324	1.00 4	3.09	6
40	MOTA	3689	CB	VAL	С	51	28.003	50.542	37.539	1.00 4	1.28	· 6
	MOTA	3690	CG1	VAL	С	51	27.355	50.017	36.267	1.00 3		6
	MOTA	3691	CG2	VAL	C	51	29.157	49.659	37.953	1.00 3		6
	MOTA	3692	С	VAL		51	27.300	52.817	36.781	1.00 4		6
4	MOTA	3693	0	VAL		51	26.385	53.163	37.522	1.00 4		8
45	MOTA	3694	Ŋ	PHE		52	27.299	53.113	35.490	1.00 4		7
	MOTA	3695	CA	PHE		52	26.206	53.883	34.937	1.00 4		6
	MOTA	3696	CB	PHE		52	26.469	55.352	35.210	1.00 4		6 6
	ATOM	3697	CG CD1	PHE		52 52	27.729 27.735	55.857 56.327	34.587 33.278	1.00 4		6
50	ATOM	3698 3699		PHE PHE		52	28.921	55.841	35.299	1.00 4		6
50	MOTA MOTA	3700		PHE		52	28.908	56.771	32.690	1.00 4		6
	ATOM	3701		PHE		52	30.102	56.284	34.722	1.00 4		6
	ATOM	. 3702	CZ	PHE		52	30.098	56.751	33.415	1.00 4		6
	ATOM	3703	C	PHE		52	26.048	53.663	33.443	1.00 4		6
55	ATOM	3704	ō	PHE		52	26.932	53.102	32.798	1.00 4	19.84	8
	MOTA	3705	N	TRP		53	24.918	54.099	32.895	1.00 4		7
	MOTA	3706	CA	TRP		53	24.684	53.985	31.471	1.00 4		6
	MOTA	3707	CB	TRP		53	23.251	53.595	31.175	1.00 4		6
00	ATOM		CG	TRP		53	22.915	52.221	31.552	1.00 4		6
60	ATOM	3709		TRP		53	21.615	51.636	31.534	1.00 5		6
	ATOM	3710	CE2	TRP	C	53	21.748	50.311	32.002	1.00.4	.y.60	6

	WO 01/58	8951							PCT/EP01/014	157
						-133				
	ATOM	3711	CE3	TRP C	53	20.342	52.106	31.170	1.00 51.64	6
	ATOM	3712		TRP C	53	23.765	51.259	32.008	1.00 48.94	6
	ATOM	3713		TRP C	53	23.073	50.107	32.284	1.00 48.58	7
_	ATOM	3714	CZ2	TRP C	53	20.659	49.448	32.120	1.00 50.24	6
5	ATOM	3715	CZ3		53	19.258	51.250	31.286	1.00 51.60	6
	ATOM	3716		TRP C	53	19.424	49.935	31.759	1.00 52.14	6
	ATOM	3717	C	TRP C	53	24.940	55.339	30.862	1.00 48.39	6
	ATOM	3718	0	TRP C	53	24.234	56.290	31.156	1.00 50.70	8
10	MOTA	3719	N	GLN C	54	25.946	55.429	30.010	1.00 49.71	7
10	ATOM ATOM	3720 3721	CA	GLN C	54	26.265	56.691	29.378	1.00 50.29	6
	ATOM	3721	CB CG	GLN C	54 54	27.759 28.231	56.749 58.111	29.053	1.00 50.27	6
	ATOM	3723	CD	GIN C	54	29.710	58.344	28.587 28.853	1.00 54.00 1.00 55.07	6 6
	MOTA	3724		GLN C	54	30.172	58.241	29.988	1.00 53.42	8
15	ATOM	3725		GLN C	54	30.458	58.667	27.805	1.00 57.05	7
	ATOM	3726	C	GLN C	54	25.415	56.797	28.125	1.00 50.70	6
	ATOM	3727	0	GLN C	54	25.886	56.617	27.004	1.00 52.15	8
	ATOM	3728	N	GLN C	55	24.138	57.069	28.345	1.00 51.37	7
	ATOM	3729	CA.	GLN C	55	23.169	57.205	27.272	1.00 54.41	6
20	ATOM	3730	CB	GLN C	55	21.786	57.326	27.897	1.00 57.18	6
	ATOM	3731	CG	GLN C	55	20.667	57.648	26.948	1.00 64.94	6
	ATOM	3732	CD	GLN C	55	19.313	57.472	27.617	1.00 70.65	6
	MOTA	3733		GLN C	55	19.154	57.760	28.817	1.00 73.87	8
0.5	ATOM	3734		GLN C	55	18.325	56.997	26.849	1.00 72.08	7
25	MOTA	3735	C	GLN C	55	23.509	58.419	26.396	1.00 53.13	6
	ATOM	3736	0	GLN C	55	23.296	59.569	26:779	1.00 54.85	8
	MOTA	3737	N	THR C	56	24.044	58.148	25.211	1.00 50.27	7
	ATOM ATOM	3738 3739	CA CB	THR C	56 56	24.455	59.193	24.290	1.00 48.20	6
30	MOTA	3740		THR C	56	25.916 26.693	59.019 58.795	23.905 25.085	1.00 47.97 1.00 51.04	6
00	ATOM	3741	CG2		56	26.431	60.243	23.219	1.00 31.04	8 6
	ATOM	3742	C	THR C	56	23.633	59.162	23.023	1.00 49.71	6
	ATOM	3743	ō	THR C	56	23.216	58.095	22.568	1.00 49.78	8
	ATOM	3744	N	THR C	57	23.393	60.340	22.454	1.00 49.24	7
35	MOTA	3745	CA	THR C	57	~ 22.619	60.436	21.221	1.00 49.62	6
	ATOM	3746	CB	THR C	57	21.122	60.592	21.501	1.00 49.45	6
	MOTA	3747	OG1	THR C	57	20.640	59.440	22.206	1.00 49.55	8
	ATOM	3748	CG2		57	20.368	60.722	20.191	1.00 51.01	6
40	ATOM	3749	C	THR C	57	23.057	61.608	20.368	1.00 48.68	6
40	ATOM	3750	0	THR C	57	23.423	62.649	20.888	1.00 51.05	8
	ATOM	3751	N	TRP C	58	23.033	61.428	19.056	1.00 45.80	7
	ATOM ATOM	3752 3753	CA CB	TRP C	58 50	23.415	62.487	18.145	1.00 45.33	6
	ATOM	3754	CG	TRP C	58 58	24.934 25.733	62.702 61.584	18.146	1.00 44.23 1.00 45.68	6
45	ATOM	3755		TRP C	58	26.221	60.428	17.556 18.241	1.00 43.51	6
	ATOM	3756		TRP C	58	26.896	59.642	17.296	1.00 41.95	6 6
	ATOM	3757		TRP C	58	26.150	59.983	19.566	1.00 44.75	6
	ATOM	3758		TRP C	58	26.120	61.453	16.264	1.00 41.99	6
	ATOM	3759	NE1	TRP C	58	26.818	60.292	16.097	1.00 43.07	7
50	ATOM	3760	CZ2	TRP C	58	27.498	58.436	17.625	1.00 42.44	6
	ATOM	3761		TRP C	58	26.748	58.778	19.894	1.00 45.66	6
	ATOM	3762		TRP C	58	27.414	58.020	18.926	1.00 44.08	6
	MOTA	3763	C	TRP C	58	22.915	62.107	16.772	1.00 46.80	6
EE	ATOM	3764	0	TRP C	58	22.315	61.054	16.603	1.00 45.26	8
55	MOTA	3765	N	SER C	59	23.157	62.959	15.788	1.00 50.21	7
	ATOM ATOM	3766	CA	SER C	59 59	22.663	62.684	14.452	1.00 53.47	6
	ATOM ATOM	3767 3768	CB OG	SER C	59 59	21.536 20.707	63.657	14.128	1.00 54.42	6
	ATOM	3769	C	SER C	59 59	23.733	63.146 62.752	13.104 13.376	1.00 59.88 1.00 54.85	8
60	ATOM	3770	Ö	SER C	59	24.541	63.682	13.343	1.00 54.85	6 8
	ATOM	3771	N	ASP C	60	23.727	61.745	12.503	1.00 57.21	7

	WO 01/5	8951									PCT	/EP01/01	1457
								-134					
	ATOM	3772		ASP	_	60		24.677	61.646	11.396	1.00		6
	MOTA	3773		ASP		60		25.680	60.517	11.650		59.62	6
	MOTA	3774		ASP		60		26.786	60.472	10.615		61.35	6
~	ATOM	3775		ASP		60		26.553	60.894	9.462	1.00		8
5	MOTA	3776		ASP		60		27.890	59.996	10.957		62.69	8
	MOTA	3777	C	ASP	-	60		23.842	61.317	10.172		61.10	. 6
	MOTA	3778	-	ASP		60		23.493	60.163	9.940		61.72	8 7
	ATOM	3779	N	ARG	-	61		23.509	62.338	9.396		63.66 65.73	6
10	MOTA	3780	CA	ARG		61 61		22.689 22.276	62.153 63.516	8.201 7.628		68.89	6
10	MOTA	3781 3782	CB CG	ARG ARG		61		21.106	64.221	8.348		74.08	6
	ATOM ATOM	3783	CD	ARG		61		20.624	65.417	7.517		79.55	6
	ATOM	3784	NE	ARG		61		19.438	66.085	8.059		84.63	7
	ATOM	3785	CZ	ARG		61		18.810	67.101	7.457		87.07	6
15	ATOM	3786		ARG		61		19.257	67.572	6.291		88.09	7
. •	ATOM	3787		ARG		61		17.721	67.636	8.005		87.40	7
	ATOM	3788	C	ARG		61		23.322	61.310	7.083	1.00	64.92	6
	ATOM	3789	0	ARG	С	61	•	22.604	60.783	6.225	1.00	65.71	8
	MOTA	3790	N	THR	С	62		24.648	61.176	7.078	1.00	62.18	7
20	ATOM	3791	CA	THR	С	62		25.301	60.393	6.038	1.00	60.64	6
	ATOM	3792	CB	THR	С	62		26.840	60.568	6.056	1.00	61.65	6
	MOTA	3793	OG1	THR		62		27.389	59.999	7.256		63.35	8
	MOTA	3794	CG2	THR		62		27.207	62.045	5.983		61.52	6
	MOTA	3795	C	THR		62		24.970	58.917	6.211		60.11	6
25	MOTA	3796	0	THR		62		25.303	58.095	5.354		61.77	8
	MOTA	3797	N	LEU		63		24.313	58.592	7.321		58.17	7
	MOTA	3798	CA	LEU		63		23.919	57.219	7.621		57.53	6
	ATOM	3799	CB	LEU		63		24.079	56.929	9.111		54.69 55.50	6 6
30	ATOM	3800	CG	LEU		63 63		25.442 25.327	57.142 56.938	9.750 11.263		54.27	6
30	ATOM ATOM	3801 3802		LEU		63		26.449	56.178	9.139		55.93	6
	ATOM	3803	CDZ	LEU		63		22.455	56.977	7.242	•	58.42	6
	ATOM	3804	0	LEU		63		22.010	55.830	7.147	1.00		8
	MOTA	3805	N	ALA		64		21.707	58.055	7.037		58.80	7
35	ATOM	3806	CA	ALA		64		20.291	57.928	6.703		61.86	6
•	ATOM	3807	CB	ALA		64		19.666	59.310	6.522	1.00	61.89	6
	ATOM	3808	C	ALA		64		20.081	57.087	5.450	1.00	63.09	6
	MOTA	3809	0	ALA	Ċ	64		20.840	57.179	4.481	1.00	63.27	8
	ATOM	3810	N	TRP		65		19.055	56.249	5.485		65.02	7
40	MOTA	3811	CA	TRP	С	65		18.749	55.381	4.355		66.31	6
	MOTA	3812	CB	TRP		65		19.329	53.989	4.600		64.14	6
	MOTA	3813	CG	TRP		65		18.597	53.208	5.687		62.22	6
	ATOM	3814		TRP		65		18.962	53.110	7.074		57.97	6
4 ~	ATOM	3815		TRP		65		18.025	52.247	7.694		56.42	6
45	MOTA	3816		TRP		65		19.985	53.666	7.848		55.52	6 6
	MOTA	3817		TRP		65		17.475	52.430 51.849	5.533 6.734		60.23 57.79	7
	MOTA	3818		TRP TRP		65 65		17.131 18.088	51.926	9.049		55.30	6
	MOTA MOTA	3819 3820		TRP		65		20.047	53.350	9.195		56.61	6
50	ATOM	3821		TRP		65		19.102	52.484	9.784		56.47	6
00	ATOM	3822	C	TRP		65		17.238	55.287	4.252		68.58	6
	ATOM	3823	ō	TRP		65		16.540	55.365	5.268		67.72	8
	ATOM	3824	N	ASN		66		16.728	55.113	3.037		72.17	7
	ATOM	3825	CA	ASN		66		15.283	55.011	2.882		75.21	6
55	ATOM	3826	CB	ASN		66		14.863	55.013	1.408		77.34	· 6
	ATOM	3827	CG	ASN		66		13.355		1.244		79.16	6
	ATOM	3828	OD1	ASN		66		12.845	55.261	0.119		80.81	8
	ATOM	3829	ND2	ASN		66		12.633	55.267	2.374		77.07	7
	MOTA	3,830	С	ASN		66		14.802	53.730	3.532		74.77	6
60	ATOM	3831	0	ASN		66		15.431	52.675	3.383		75.31	8
	MOTA	3832	N	SER	С	67		13.685	53.816	4.244	1.00	73.52	7

	WO 01/58	8951							•	PCT/EP01/0	1457
							-135				
	ATOM	3833	CA	SER	C.	67	13.166	52.647	4.920	1.00 73.52	,6
	ATOM	3834	CB	SER		67	13.451	52.759	6.411	1.00 72.63	6
	ATOM	3835	OG	SER	С	67	12.985	53.994	6.914	1.00 70.04	8
_	MOTA	3836	C	SER		67	11.684	52.469	4.702	1.00 75.29	6
5	ATOM	3837	0	SER		67	11.010	51.788	5.493	1.00 75.31	8
	ATOM	3838	N	SER		68	11.165	53.077	3.639	1.00 77.57	. 7
	ATOM	3839	CA	SER		68	9.739	52.957	3.356	1.00 78.39	6
	MOTA	3840	CB	SER		68	9.327	53.874	2.187	1.00 77.79	6
10	ATOM ATOM	3841 3842	OG C	SER SER		68 68	10.010 9.398	53.570 51.498	0.983 3.051	1.00 77.16 1.00 78.91	8 6
.0	ATOM	3843	0	SER		68	8.242	51.165	2.802	1.00 78.88	8
	ATOM	3844	N	HIS		69	10.415	50.634	3.090	1.00 80.17	7
٠	ATOM	3845	CA	HIS		69	10.252	49.197	2.824	1.00 81.55	6
	MOTA	3846	CB	HIS		69	10.307	48.935	1.319	1.00 84.67	6
15	MOTA	3847	CG	HIS	С	69	9.327	49.755	0.542	1.00 88.75	6
	ATOM	3848		HIS		69	8.119	49.436	0.014	1.00 89.38	6
	MOTA	3849		HIS		69	9.479	51.115	0.359	1.00 89.98	7
	ATOM	3850		HIS		69	8.405	51.600	-0.239	1.00 91.29	6
20	ATOM	3851		HIS		69	7.564	50.602	-0.458	1.00 91.72	7
20	ATOM	3852	C	HIS HIS		69 69	11.363 11.740	48.406 47.318	3.514	1.00 80.62	6
	ATOM ATOM	3853 3854	O N	SER		70	11.740	47.318	3.072 4.614	1.00 79.15 1.00 79.62	8 7
	ATOM	3855	CA	SER		70	12.950	48.341	5.355	1.00 77.30	6
	ATOM	3856	CB	SER		70	14.262	48.818	4.739	1.00 77.47	6
25	ATOM	3857	OG	SER		70	14.107	48.991	3.336	1.00 74.00	8
	ATOM	3858	C	SER		70	12.880	48.746	6.836	1.00 76.56	6
	ATOM	3859	0	SER	С	70	12.168	49.686	7.193	1.00 77.11	8
	ATOM	3860	N	PRO	С	71	13.587	48.014	7.726	1.00 76.29	7
	ATOM	3861	CD	PRO		71	14.305	46.733	7.544	1.00 75.52	6
30	MOTA	3862	CA	PRO		71	13.538	48.401	9.143	1.00 74.74	6
	ATOM	3863	CB	PRO		71	14.366	47.322	9.843	1.00 75.26	6
	MOTA	3864	CG	PRO		71	14.241	46.124	8.936	1.00 75.64	6
	MOTA MOTA	3865 3866	С 0	PRO PRO		71	14.202 15.042	49.771 50.125	9.235 8.401	1.00 73.61 1.00 72.22	6
35	ATOM	3867	Ŋ	ASP		72	13.828	50.123	10.247	1.00 72.22	8 7
•	ATOM	3868	CA	ASP		72	14.377	51.869	10.414	1.00 72.00	6
	ATOM	3869	СВ	ASP		72	13.277	52.795	10.899	1.00 75.25	6
	ATOM	3870	CG	ASP		72	11.919	52.353	10.415	1.00 78.33	6
	MOTA	3871	OD1	ASP	С	72	11.633	52.512	9.199	1.00 79.88	8
40	MOTA	3872	OD2	ASP	С	72	11.150	51.821	11.256	1.00 79.56	8
	MOTA	3873	С	ASP		72	15.519	51.835	11.411	1.00 68.36	6
	ATOM	3874	0	ASP		72	16.046	52.887	11.799	1.00 66.88	8
	MOTA	3875	N	GLN		73	15.883	50.625	11.838	1.00 63.81	7
45	MOTA	3876	CA	GLN		73	17.001	50.485	12.756	1.00 61.20	6
70	ATOM ATOM	3877 3878	CB CG	GLN GLN		73 73	16.537 16.121	50.494	14.191	1.00 61.12 1.00 62.71	6
	ATOM	3879	CD	GLN		73	15.665	51.802 51.603	14.749 16.163	1.00 62.71	6 6
	ATOM	3880	OE1			73	14.784	50.779	16.421	1.00 67.49	8
	ATOM	3881	NE2			73	16.267	52.329	17.099	1.00 66.00	7
50	ATOM	3882	С	GLN		73	17.842	49.232	12.583	1.00 59.70	6
	ATOM	3883	0	GLN	С	73	17.350	48.167	12.213	1.00 61.26	8
	ATOM	3884	N	VAL		74	19.122	49.369	12.893	1.00 56.05	7
	MOTA	3885	CA	VAL		74	20.050	48.260	12.825	1.00 52.11	6
55	ATOM	3886	CB CC1	VAL		74	20.736	48.177	11.454	1.00 52.42	6
55	ATOM	3887		VAL		74 74	19.732	47.788	10.397	1.00 51.61	6
	ATOM ATOM	3888 3889	CGZ	VAL VAL		74 74	21.376 21.095	49.507 48.498	11.112 13.891	1.00 52.96 1.00 50.29	6 6
	ATOM	3890	0	VAL		74	21.277	49.626	14.332	1.00 30.29	8
	ATOM	3891	N	SER		75	21.754	47.431	14.323	1.00 49.79	7
60	ATOM	3892	CA	SER		75	22.809	47.533	15.318	1.00 45.56	6
	MOTA	3893	CB	SER		75	22.784	46.337	16.257	1.00 43.40	6

	WO 01/58	951							PCT/EP01/0	1457
						-136				
	ATOM	3894	OG	SER C	75		46.521	17.269	1.00 43.9	9 8
	MOTA	3895	C	SER C	75	24.146	47.611	14.595	1.00 44.8	
	MOTA	3896	0	SER C	75	24.519	46.703	13.858	1.00 47.6	
_	MOTA	3897	N	VAL C	76	24.858	48.712	14.811	1.00 43.5	
5	ATOM	3898	CA	VAL C	76	26.140	48.941	14.165	1.00 42.8	4 6
	ATOM	3899	CB	VAL C	76	26.122	50.273	13,412	1.00 41.7	
	MOTA MOTA	3900 3901		VAL C	76	27.441	50.504	12.741	1.00 42.7	
	ATOM	3901	CGZ	VAL C	76 76	25.003	50.279	12.403	1.00 40.7	
10	ATOM	3903	Ö	VAL C	76	27.294 27.194	48.961 49.542	15.153 16.227	1.00 42.6 1.00 45.7	-
	ATOM	3904	Ŋ	PRO C	77	28.409	48.313	14.812	1.00 45.7	
	ATOM	3905	CD	PRO C	77	28.644	47.345	13.737	1.00 41.7	
	ATOM	3906	CA	PRO C	77	29.532	48.326	15.748	1.00 41.6	
	MOTA	3907	CB	PRO C	77	30.527	47.370	15.108	1.00 40.4	
15	MOTA	3908	CG	PRO C	77	29.654	46.432	14.379	1.00 42.4	
	ATOM	3909	С	PRO C	77	30.074	49.746	15.860	1.00 41.2	9 6
	MOTA	3910	0	PRO C	77	30.123	50.489	14.881	1.00 38.6	
	MOTA MOTA	3911	N	ILE C	78	30.469	50.111	17.070	1.00 41.8	
20	ATOM	3912 3913	CA	IFE C	78 78	31.000 31.439	51.433	17.359	1.00 41.9	
	ATOM	3914	CG2		78	32.370	51.489 52.634	18.837 19.107	1.00 42.1 1.00 42.1	
	ATOM	3915		ILE C	78	30.193	51.601	19.696	1.00 44.7	_
	MOTA	3916		ILE C	78	29.251	52.676	19.216	1.00 44.1	
	ATOM	3917	С	ITE C	78	32.149	51.813	16.450	1.00 42.5	7 6
25	MOTA	3918	0	ILE C	78	32.287	52.963	16.063	1.00 45.1	
	MOTA	3919	N	SER C	79	32.963	50.829	16.100	1.00 43.1	
	ATOM	3920	CA	SER C	79	34.120	51.030	15.241	1.00 43.5	
	ATOM	3921	CB	SER C	79	34.969	49.768	15.242	1.00 43.7	
30	ATOM ATOM	3922 3923	OG C	SER C	79 79	34.189	48.637	14.910	1.00 43.5	
00	ATOM	3923	. 0	SER C	79 79	33.810 34.698	51.415 51.838	13.804 13.082	1.00 43.4	
	ATOM	3925	N	SER C	80	32.562	51.264	13.380	1.00 44.1 1.00 43.6	
	MOTA	3926	CA	SER C	-80	32.180	51.604	12.012	1.00 44.8	
	ATOM	3927	CB	SER C	80	31.260	50.534	11.441	1.00 44.2	
35	MOTA	3928	OG	SER C	80	31.915	49.284	11.380	1.00 52.5	
	MOTA	3929	C	SER C	80	31.482	52.956	11.908	1.00 46.5	7 6
	ATOM	3930	0	SER C	80	31.050	53.355	10.829	1.00 46.1	
	ATOM	3931 3932	N	LEU C	81	31.366	53.649	13.035	1.00 46.4	•
40	ATOM ATOM	3932	CA CB	FER C	81 81	30.720 29.467	54.952	13.080	1.00 45.8	
	MOTA	3934	CG	PEO C	81	28.421	54.891 53.827	13.935 13.653	1.00 45.00	
	ATOM	3935		LEU C	81	27.488	53.701	14.839	1.00 45.0	
	MOTA	3936		LEU C	81	27.667	54.198	12.405	1.00 47.69	
	ATOM	3937	С	LEU C	81	31.645	55.973	13.718	1.00 46.1	
45	ATOM	3938	0	TEA C	81	32.636	55.613	14.355	1.00 50.3	
	MOTA	3939	N	TRP C	82	31.323	57.249	13.536	1.00 43.5	3 7
	MOTA	3940	CA	TRP C	82	32.086	58.303	14.161	1.00 39.79	
	MOTA MOTA	3941 3942	CB	TRP C	82	31.860	59.639	13.463	1.00 41.90	
50	ATOM	3943	CD2	TRP C	82 82	32.342 31.577	60.817 <b>61.</b> 569	14.278	1.00 44.13	
••	ATOM	3944		TRP C	82	32.453	62.504	15.230 15.823	1.00 44.19	
	ATOM	3945		TRP C	82	30.234	61.540	15.645	1.00 44.58	3 6
	ATOM	3946	CD1	TRP C	82	33.611	61.318	14.327	1.00 43.74	
	MOTA	3947		TRP C	82	33.686	62.327	15.252	1.00 44.54	
55	ATOM	3948		TRP C	82	32.033	63.405	16.809	1.00 42.68	3 6
	MOTA	3949		TRP C	82	29.818	62.430	16.623	1.00 43.22	6
	MOTA	3950	CH2		82	30.717	63.352	17.195	1.00 43.77	
	MOTA MOTA	3951 3952	C O	TRP C	82 82	31.426	58.348	15.514	1.00 40.00	
60	ATOM	3953	N	VAL C	82 83	30.219 32.201	58.174 58.574	15.619 16.557	1.00 39.36	_
- <del>-</del>	ATOM	3954	CA	VAL C	83	31.626	58.649	16.557 17.887	1.00 40.23 1.00 39.34	
				_	-			_,,,,,,,		

	WO 01/5	8951								PCT/EP01/01	1457
							-137				
	MOTA	3955		VAL		83	31.891	57.325	18.657	1.00 38.82	6
	MOTA	3956		VAL		83	31.587	57.479	20.109 18.087	1.00 39.50 1.00 38.81	· 6
	ATOM	3957		VAL		83	31.021	56.219 59.860	18.624	1.00 40.30	6
5	MOTA	3958	C	VAL VAL		83 83	33.365	60.222	18.428	1.00 40.30	8
3	MOTA ATOM	3959 3960	N O	PRO		84	31.386	60.528	19.451	1.00 38.82	7
	ATOM	3961	CD	PRO		84	29.948	60.288	19.644	1.00 40.83	6
	ATOM	3962	CA	PRO		84	31.812	61.698	20.220	1.00 36.19	6
	ATOM	3963	СВ	PRO		84	30.580	62.022	21.058	1.00 37.66	6
10	ATOM	3964	CG	PRO		84	29.479	61.609	20.201	1.00 39.39	6
	MOTA	3965	С	PRO	С	84	32.999	61.358	21.098	1.00 34.25	6
	MOTA	3966	0	PRO		84	32.987	60.351	21.788	1.00 35.16	8
	MOTA	3967	N	ASP		85	34.016	62.206	21.093	1.00 33.39	7
4-	MOTA	3968	CA	ASP		85	35.192	61.949	21.909	1.00 34.67	6
15	MOTA	3969	CB	ASP		85	36.423 36.260	62.588 64.056	21.270 21.046	1.00 35.95 1.00 35.70	6 6
	MOTA	3970 3971	CG	ASP ASP		85 85	35.159	64.468	20.662	1.00 33.70	8
	ATOM ATOM	3971		ASP		85	37.234	64.798	21.238	1.00 38.52	8
	ATOM	3972	C	ASP		85	35.005	62.452	23.326	1.00 36.34	6
20	MOTA	3974	Ö	ASP		85	35.806	63.229	23.841	1.00 39.41	8
	ATOM	3975	Ŋ	LEU		86	33.941	61.978	23.962	1.00 36.11	7
	ATOM	3976	CA	LEU	С	86	33.609	62.385	25.315	1.00 36.00	6
	MOTA	3977	CB	LEU	С	86	32.208	61.904	25.678	1.00 35.07	6
	MOTA	3978	CG	LEU		86	31.089	62.464	24.806	1.00 36,71	6
25	ATOM	3979		LEU		86	29.752	61.912	25.240	1.00 31.87	6
	MOTA	3980		LEU		86	31.112	63.974	24.910	1.00 35.41	6
	ATOM	3981	G .	LEU		86	34.585	61.870	26.337 26.189	1.00 36.89 1.00 38.19	6 8
	MOTA	3982 3983	0	LEU ALA		86 87	35.147 34.773	60.795 62.648	27.391	1.00 38.71	7
30	MOTA MOTA	3984	N CA	ALA		87	35.672	62.268	28.461	1.00 38.06	6
00	ATOM	3985	CB	ALA		87	37.045	62.838	28.200	1.00 35.59	6
	ATOM	3986	C	ALA		87	35.119	62.799	29.772	1.00 38.10	6
	ATOM	3987	ō	ALA		87	34.586	63.891	29.815	1.00 37.91	8
	ATOM	3988	N	ALA		88	35.217	62.013	30.833	1.00 39.52	7
35	MOTA	3989	CA	ALA		88	34.756	62.448	32.147	1.00 40.05	6
	ATOM	3990	CB	ALA		88	34.356	61.250	33.005	1.00 40.30	6
	ATOM	3991	C	ALA	_	88	35.939	63.169	32.771	1.00 41.63	6 8
	MOTA	3992	0	ALA		88	36.912	62.545	33.195 32.799	1.00 41.71 1.00 42.71	7
40	MOTA	3993	N CA	TYR TYR		89 89	35.852 36.904	64.492 65.350	33.330	1.00 41.60	6
40	ATOM ATOM	3994 3995	CB	TYR		89	36.368	66.775	33.459	1.00 43.41	6
	MOTA	3996	CG	TYR		89	35.976	67.422	32.149	1.00 48.68	6
	MOTA	3997		TYR		89	35.321	68.653	32.129	1.00 51.90	6
	ATOM	3998		TYR		89	34.991	69.284	30.920	1.00 53.01	6
45	ATOM	3999	CD2	TYR	С	89	36.290	66.830	30.929	1.00 48.32	6
	MOTA	4000	CE2	TYR		89	35.966	67.449	29.726	1.00.52.45	6
	MOTA	4001	CZ	TYR		89	35.318	68.678	29.730	1.00 53.45	6
	MOTA	4002	OH	TYR		89	35.017	69.305	28.545	1.00 56.75	8
<b>E</b> 0	MOTA	4003	C	TYR		89	37.527	64.914	34.657	1.00 40.68 1.00 39.21	6
50	ATOM	4004	0	TYR ASN		89 90	38.727 36.725		34.863 35.562	1.00 39.53	8 7
	MOTA MOTA	4005 4006	N CA	ASN		90	37.265	63.952	36.848	1.00 39.15	6
	ATOM	4007	CB	ASN		90	36.476		37.989	1.00 38.99	· 6
	ATOM	4008	CG	ASN		90	34.995		37.944	1.00 38.22	6
55	ATOM	4009		ASN		90	34.355		36.902	1.00 37.33	8
	ATOM	4010		ASN		90	34.443	63.939	39.090	1.00 39.59	7
	MOTA	4011	С	ASN		90	37.343		37.033	1.00 41.22	6
	MOTA	4012	0	ASN		90	37.354		38.153	1.00 42.78	8
60	MOTA	4013	N	ALA		91	37.400		35.915	1.00 42.37	7.
60	MOTA	4014	CA	ALA		91	37.528		35.928 34.521	1.00 40.71 1.00 41.88	6 6
	MOTA	4015	CB	ALA	Ü	91	37.346	59.733	J4.J4I	T'00 #T'00	O

	WO 01/5	8951							PCT/EP01/0	1457
						-138				
	ATOM ATOM	4016 4017	С 0	ALA C	91 91	38.939 39.898	60.033 60.664	36.435 36.007	1.00 39.96 1.00 35.60	6 8
	ATOM	4017	N	ILE C	92	39.040	59.093	37.356	1.00 35.80	7
	ATOM	4018	CA	ILE C	92	40.292	58.731	37.330	1.00 41.49	6
5	ATOM	4020	CB	ILE C	92	40.020	58.594	39.511	1.00 47.77	6
Ŭ	ATOM	4021	CG2	ILE C	92	39.923	57.130	39.921	1.00 48.36	6
	ATOM	4022	CG1		92	41.093	59.293	40.316	1.00 50.98	6
	ATOM	4023		ILE C	92	40.903	59.036	41.812	1.00 55.36	6
	ATOM	4024	С	ILE C	92	40.861	57.416	37.403	1.00 41.81	6
10	ATOM	4025	0	ILE C	92	41.973	56.992	37.720	1.00 40.19	8
	ATOM	4026	N	SER C	93	40.080	56.781	36.541	1.00 39.24	7
	MOTA	.4027	CA	SER C	93	40.470	55.534	35.913	1.00 39.09	6
	ATOM	4028	CB	SER C	93	39.892	54.356	36.685	1.00 39.19	6
	ATOM	4029	OG	SER C	93	38.479	54.310	36.541	1.00 39.34	8
15	MOTA	4030	С	SER C	93	39.839	55.579	34.546	1.00 37.69	6
	ATOM	4031	0	SER C	93	38.987	56.404	34.311	1.00 39.27	8
	ATOM	4032	N	LYS C	94	40.251	54.717	33.632	1.00 37.58	7
	ATOM ATOM	4033 4034	CA CB	LYS C	94 94	39.612 40.560	54.737 54.256	32.330 31.228	1.00 40.65 1.00 41.66	6 6
20	ATOM	4034	CG	LYS C	94	41.383	53.024	31.520	1.00 41.00	
20	ATOM	4036	CD	LYS C	94	42.502	52.902	30.485	1.00 48.62	
	ATOM	4037	CE	LYS C	94	41.962	53.091	29.069	1.00 47.90	
	ATOM	4038	NZ	LYS C	94	42.999	52.929	28.024	1.00 48.05	
	ATOM	4039	С	LYS C	94	38.321	53.926	32.359	1.00 40.78	
25	MOTA	4040	0	LYS C	94	38.102	53.094	33.234	1.00 42.52	
	MOTA	4041	N	PRO C	95	. 37.434	54.178	31.404	1.00 41.55	
	MOTA	4042	CD	PRO C	95	37.555	55.150	30.312	1.00 42.12	
	ATOM	4043	CA	PRO C	95	36.153	53.479	31.335	1.00 41.34	
30	MOTA MOTA	4044 4045	CB	PRO C	95 95	35.439 36.125	54.166 55.476	30.177 30.058	1.00 41.08 1.00 42.87	
50	ATOM	4045	C	PRO C	95	36.256	52.000	31.102	1.00 42.87	
	ATOM	4047	ō	PRO C	95	36.941	51.563	30.189	1.00 41.65	
	ATOM	4048	N	GLU C	96	35.581	51.228	31.940	1.00 40.55	
	MOTA	4049	CA	GLU C	96	35.560	49.791	31.766	1.00 41.10	6
35	MOTA	4050	CB	GLU C	96	35.684	49.050	33.104	1.00 43.71	
	ATOM	4051	CG	GLU C	96	35.762	47.521	32.954	1.00 49.85	
	ATOM	4052	CD	GLU C	96	35.912	46.768	34.286	1.00 54.35	
	ATOM	4053	OE1 OE2		96	36.282 35.682	47.404 45.534	35.302 34.316	1.00 58.62 1.00 52.48	
40	ATOM ATOM	4054 4055	C	GLU C	96 96	34.190	49.553	31.168	1.00 32.48	
40	ATOM	4056	Ö	GTO C	96	33.200	49.478	31.894	1.00 40.62	
	ATOM	4057	N	VAL C	97	34.133	49.483	29.841	1.00 35.73	
	ATOM	4058	CA	VAL C	97	32.876	49.249	29.153	1.00 34.27	
	ATOM	4059	CB	VAL C	97	33.006	49.541	27.660	1.00 31.66	6
45	ATOM	4060		VAL C	97	31.686	49.333	26.968	1.00 34.09	
	MOTA	4061		VAL C	97	33.437	50.963	27.470	1.00 30.22	
	ATOM	4062	C	VAL C	97	32.481	47.801	29.382	1.00 34.55	
	ATOM	4063	0	VAL C		33.167	46.891	28.949	1.00 35.63	
50	MOTA MOTA	4064 4065	N CA	LEU C	98 98	31.362 30.868	47.607 46.286	30.072 30.433	1.00 35.35 1.00 34.12	
00	ATOM	4066	CB	LEU C	98	30.098	46.377	31.752	1.00 33.63	
	MOTA	4067	CG	LEU C	98	30.741	47.049	32.961	1.00 35.44	
	MOTA	4068		LEU C	98	29.694	47.352	33.989	1.00 37.77	
_, _	MOTA	4069		LEU C	98	31.806	46.166	33,538	1.00 34.23	6
55	MOTA	4070	C	LEU C	98	29.965	45.641	29.404	1.00 36.94	
	ATOM	4071	0	LEU C	98	29.640	44.464	29.524		
	MOTA	4072	N	THR C	99	29.567	46.398	28.389	1.00 36.94	
	ATOM ATOM	4073 4074	CA CB	THR C	99 99	28.642 27.317	45.881 46.674	27.393 27.450	1.00 36.72 1.00 36.81	
60	ATOM	4075		THR C		27.574	48.076	27.259	1.00 40.25	
	ATOM	4076		THR C	99	26.648	46.474	28.792	1.00 34.14	

	WO 01/58	951								PCT/	<b>EP</b> 01/01	<b>457</b>
							-139					
	» ШОМ	4077		mun	_	99	29.154	45.895	25 065	1 00	37.65	6
	ATOM ATOM	4077 4078	С 0	THR		99	30.147	46.549	25.965 25.664		37.93	8
	ATOM	4079	N	PRO		100	28.497	45.134	25.004		37.89	7
	ATOM	4080	CD	PRO			27.443	44.145	25.364		40.71	6
5	ATOM	4081	CA	PRO			28.874	45.065	23.667		37.03	6
Ŭ,	ATOM	4082	CB	PRO			27.716	44.298	23.046		37.46	6
	ATOM	4083	CG	PRO			27.402	43.316	24.094		38.27	6
	ATOM	4084	C	PRO			28.963	46.476	23.139		38.41	6
	ATOM	4085	Ō	PRO			28.082	47.297	23.390		39.24	8
10	ATOM	4086	N	GLN			30.026	46.772	22.412	1.00	38.06	7
	ATOM	4087	CA	GLN			30.169	48.113	21.893	1.00	39.24	6
	ATOM	4088	CB	GLN	C	101	31.639	48.479	21.827	1.00	38.35	6
	ATOM	4089	CG	GLN	С	101	32.140	48.846	23.195	1.00	43.58	6
	ATOM	4090	CD	GLN	С	101	33.633	48.822	23.291	1.00	47.06	6
15	ATOM	4091	OE1	GLN			34.315	49.497	22.533		51.61	8
	ATOM	4092	NE2				34.160	48.041	24.227		48.13	7
	ATOM	4093	С	GLN			29.471	48.333	20.571		38.37	6
	MOTA	4094	0	GLN			30.095	48.620	19.554		36.55	8
20	ATOM	4095	N	LEU			28.148	48.198	20.627		40.04	7
20	MOTA	4096	CA	LEU			27.263	48.373	19.478		40.82	6
	ATOM	4097	CB.	LEU			26.376	47.143	19.289		38.65	6
	MOTA MOTA	4098 4099	CG	LEU			27.061 26.015	45.791	19.163		40.16 37.69	6 6
	ATOM	4100		LEU			27.991	44.708 45.815	18.994 17.981		39.89	6
25	ATOM	4100	CDZ	LEU			26.362	49.583	19.685		40.48	6
_0	ATOM	4102	0	LEU			25.940	49.880	20.800		39.50	8
	ATOM	4103	N	ALA			26.072	50.280	18.603		40.58	7
	ATOM	4104	CA	ALA			25.203	51.434	18.674		42.17	6
	ATOM	4105	СВ	ALA			25.879	52.646	18.054		43.90	6
30	MOTA	4106	C	ALA			23.950	51.087	17.904		43.55	6
	MOTA	4107	0	ALA			23.905	50.092	17.189	1.00	44.89	8
	ATOM	4108	N	ARG	С	104	22.930	51.916	18.048	1.00	45.38	7
	MOTA	4109	CA	ARG			21.674	51.689	17.359	1.00	46.54	6
	MOTA	4110	CB	ARG	С	104	20.549	51.665	18.381	100	46.10	б
35	ATOM	4111	CG	ARG			19.292	51.040	17.879		47.91	6
	ATOM	4112	CD	ARG			19.457	49.560	17.559		45.29	6
	ATOM	4113	NE	ARG			18.188	49.059	17.035		46.68	7
	ATOM	4114	CZ	ARG			17.927	47.792	16.761		46.66	6
40	MOTA	4115		ARG			18.850	46.866	16.954		47.05	7
40	MOTA MOTA	4116 4117		ARG ARG			16.733 21.491	47.452	16.308 16.367		48.97	7
	ATOM	4117	0	ARG	_	_	21.550	53.999	16.738		49.29	6 8
	ATOM	4119	N	VAL			21.296	52.501	15.098		47.65	7
	ATOM	4120	CA	VAL			21.138	53.543	14.092		47.99	6
45	MOTA	4121	CB	VAL			22.200	53.426	12.980		46.29	6
	ATOM	4122		VAL			22.080	54.588	12.021		44.96	6
	ATOM	4123		VAL			23.583	53.386	13.580		42.95	6
	ATOM	4124	С	VAL			19.769	53.519	13.444		50.20	6
	ATOM	4125	0	VAL	C	105	19.340	52.497	12.904	1.00	50.01	8
50	MOTA	4126	N	VAL	C	106	19.097	54.666	13.506	1.00	51.90	7
	ATOM	4127	CA	VAL			17.767	54.836	12.933		53.33	6
	MOTA	4128	CB	VAL			16.947	55.840	13.758		51.93	6
	ATOM	4129		VAL			15.503	55.825	13.306		49.94	6.
EE	ATOM	4130		VAL			17.060	55.504	15.222		50.56	6
55	MOTA	4131	C	VAL			17.899	55.347	11.497		53.76	6
	ATOM	4132	0	VAL			18.782	56.151	11.203		52.33	8
	ATOM	4133 4134		SER			17.016	54.889	10.615 9.208		54.08 56.13	7
	ATOM ATOM	4134	CA CB	SER			17.066 15.835	55.275 54.734	8.487		56.67	6 6
60	ATOM	4136	OG	SER			14.672	54.734	9.268		59.41	8
	ATOM	4137	C	SER			17.228	56.762	8.895		56.30	6
			-		-		· - <b></b>	··-				-

WO 01/58951

PCT/EP01/01457

	MO 01/2	8951								PCT/EP01/01	45/
							140				
							-140				8
	ATOM	4138		SER C			17.678	57.129	7.797	1.00 55.13	7
	ATOM	4139		ASP C			16.879	57.619	9.849	1.00 56.72	6
	MOTA	4140		ASP C			16.999	59.064	9.632	1.00 58.46	
	MOTA	4141		ASP C			15.875	59.807	10.353	1.00 59.64	6
5	MOTA	4142		ASP C			15.998	59.735	11.856	1.00 60.59	6 (
	ATOM	4143		ASP C			16.432	58.693	12.378	1.00 61.80	8
	MOTA	4144	OD2	ASP C			15.643	60.724	12.520	1.00 63.04	8
	ATOM	4145	С	ASP C			18.345	59.648	10.054	1.00 58.38	6
	ATOM	4146	0	ASP C			18.513	60.859	10.068	1.00 58.33	8
10	MOTA	4147	N	GLY C			19.299	58.785	10.396	1.00 59.41	7
	MOTA	4148	CA	GLY C			20.618	59.246	10.786	1.00 58.66	6
	MOTA	4149	С	GLY C			20.802	59.467	12.271	1.00 59.58	6
	MOTA	4150	0	GLY C			21.868	59.926	12.695	1.00 59.07	8 7
	MOTA	4151	N		110		19.775	59.165	13.064	1.00 59.04	
15	MOTA	4152	CA	GLU C			19.871	59.325	14.508	1.00 59.38	6 '
	MOTA	4153	CB	GLU C			18.481	59.327	15.141	1.00 62.39	6
	MOTA	4154	CG	GLU C			18.386	60.020	16.513	1.00 66.23 1.00 70.42	6 6
	MOTA	4155	CD	GLU C			18.717	61.520	16.441	1.00 70.42	8
	MOTA	4156					18.640	62.107	15.333	1.00 69.27	8
20	ATOM	4157	OE2	GLU C			19.047	62.117	17.493	1.00 72.23	6
	MOTA	4158	C	GLU C			20.677	58.141	15.038	1.00 60.95	8
	MOTA	4159	0	GLU C			20.467	56.995 58.419	14.623 15.953	1.00 57.63	7
	MOTA	4160	Ŋ	VAL C			21.600 22.444	57.379	16.535	1.00 57.03	6
0.5	MOTA	4161	CA	VAL C			23.926	57.620	16.200	1.00 55.71	6
25	MOTA	4162	CB	VAL C			24.783	56.511	16.788	1.00 53.71	6
	MOTA	4163		VAL C			24.705	57.706	14.686	1.00 56.04	6
	MOTA	4164		VAL C			22.308	57.7337	18.048	1.00 54.63	6
	MOTA	4165 4166	C	VAL C			22.328	58.373	18.706	1.00 53.67	8
30	MOTA	4166	N O	LEU C			22.171	56.137	18.596	1.00 53.09	7
30	MOTA MOTA	4168	CA	LEU C			22.050	55.992	20.034	1.00 53.62	6
	ATOM	4169	CB	LEU C			20.638	55.548	20.420	1.00 56.64	6
	MOTA	4170	CG	LEU C			19.380	56.011	19.657	1.00 60.85	6
	MOTA	4171		LEU C			19.439	57.490	19.341	1.00 62.41	6
35	MOTA	4172		LEU C			19.244	55.207	18.374	1.00 62.32	6
00	MOTA	4173	C	LEU C			23.053	54.963	20.542	1.00 53.28	6
	MOTA	4174	0	LEU C			23.024	53.807	20.134	1.00 54.91	8
	MOTA	4175	N	TYR C			23.943	55.389	21.429	1.00 50.87	7
	ATOM	4176	CA	TYR C			24.947	54.502	22.003	1.00 47.87	6
40	MOTA	4177	CB	TYR C	113		26.362	54.924	21.560	1.00 44.85	6
	MOTA	4178	CG	TYR C	113		27.500	54.099	22.134	1.00 40.84	6
	MOTA	4179	CD1	TYR C	113		27.428	52.716	22.181	1.00 39.92	6
	MOŢA	4180		TYR C			28.481	51.956	22.679	1.00 39.26	6
	MOTA	4181		TYR C			28.663	54.710	22.602	1.00 41.11	6
45	ATOM	4182	CE2	TYR C			29.720	53.962	23.100	1.00 40.68	6
	MOTA	4183	CZ	TYR C			29.625	52.583	23.138	1.00 41.46	6
	ATOM	4184	OH	TYR C			30.667	51.831	23.649	1.00 40.70	8
	MOTA	4185	С	TYR C			24.805	54.611	23.508	1.00 48.03 1.00 47.83	6 8
	MOTA	4186	0	TYR C			25.002	55.673	24.089 24.146	1.00 47.83	7
50	ATOM	4187	N	MET C			24.457	53.508	25.583	1.00 49.26	6
	MOTA	4188	CA	MET C			24.283 22.809	53.519 53.375	25.910	1.00 43.20	6
	MOTA	4189	CB	MET C				53.558	27.370	1.00 58.33	6
	MOTA	4190	CG	MET C			22.494	52.927	27.696	1.00 50.33	16
E E	MOTA	4191		MET C			19.859	54.330	27.098	1.00 65.99	6
55	MOTA	4192	CE	MET C			25.055	52.393	26.244		6
	ATOM	4193	C	MET (			24.485	51.360	26.579		8
	ATOM ATOM	4194 4195		PRO (			26.364	52.576	26.440		7
	MOTA	4195		PRO (			27.181	53.711	25.976		6
60		4197			115		27.207	51.556	27.066		6
	MOTA	4198			115	•	28.591	51.903	26.545		6
									•		

							-141							
	ATOM	4199	CG	PRO (	2 11	5	28.5		53.39	98 2	6.559	1.00	48.59	6
	ATOM	4200	C	PRO (			27.1		51.63		8.585		48.68	6
	ATOM	4201	ō	PRO (			26.9		52.72		9.142		48.78	8
	ATOM	4202	N	SER			27.2		50.49		9.249	1.00	47.05	7
5	ATOM	4203	CA	SER			27.2		50.48		0.699	1.00	45.85	6
•	ATOM	4204	СВ	SER			26.7		49.1		1.248	1.00	45.70	6
	ATOM	4205	OG	SER			26.7		49.22	28 3	2.667	1.00	46.59	8
	MOTA	4206	c	SER			28.7		50.60		1.097	1.00	47.30	6
	ATOM	4207	Ō	SER			29.5		49.79		0.695		48.38	8
10	MOTA	4208	N	ILE			29.0	58	51.62	22 3	1.892	1.00	45.86	7
	ATOM	4209	CA	ILE			30.4		51.84		2.293	1.00	41.61	6
	MOTA	4210	CB	ILE		.7	30.9	26	53.23	10 3	1.749	1.00	39.60	6
	ATOM	4211	CG2	ILE			32.3	25	53.49	99 3	2.230	1.00	38.47	6
	ATOM	4212	CG1	ILE			30.8	76	53.20	08 3	0.225	1.00	38.60	6
15	ATOM	4213	CD1	ILE	C 11	.7	31.0	25	54.5	63 2	9.619	1.00	34.54	6
	ATOM	4214	С	ILE	C 11	.7	30.7	80	51.83	30 3	3.796	1.00	42.04	6
	MOTA	4215	0	ILE	C 11	7	29.9	48	52.3	90 3	4.587	1.00	42.87	8
	MOTA	4216	N	ARG	C 11	.8	31.7	87	51.1	58 3	4.182	1.00	40.79	7
	MOTA	4217	CA	ARG	C 11	8	32.2	10	51.1	62 3	5.568	1.00	40.35	6
20	MOTA	4218	CB.	ARG			32.6	07	49.7	82 3	6.060	1.00	37.23	6
	MOTA	4219	CG	ARG	C 11	8	33.1	.72	49.8	66 3	7.455	1.00	36.55	6
	ATOM	4220	CD	ARG	C 11	8	33.2	77	48.5	38 3	8.156	1.00	39.03	6
	MOTA	4221	NE	ARG	C 11	L8	33.8	74	48.6	93 3	9.483	1.00	39.42	. 7
	MOTA	4222	CZ	ARG	C 11	L8	33.8	82	47.7	56 4	0.424		39.50	6
25	MOTA	4223	NH1	ARG	C 11	<b>.</b> 8	33.3	26	46.5	74 4	0.208		40.01	7
	MOTA	4224	NH2	ARG	C 13	18	34.4	34	48.0	12 4	1.594	_	40.75	7
	MOTA	4225	С	ARG	C 11	L8	33.4	40	52.0	65 3	5.545		41.99	6
	MOTA	4226	0	ARG			34.3		51.8		4.722		43.88	8
	MOTA	4227	N	GLN			33.5		53.0		6.436		42.79	7
30	MOTA	4228	CA	GLN			34.6		53.9		6.408		43.05	6
	MOTA	4229	CB	GLN			34.4		54.9		5.252		41.88	6
	MOTA	4230	CG	GLN			35.5		55.9		5.034		41.06	6
	MOTA	4231	CD	GLN			35.2		56.6		3.732		41.03	6
	MOTA	4232		GLN			34.1		56.8		3.331		40.46	8
35	MOTA	4233	NE2	GLN			36.3		57.0		3.066		43.78	7
	MOTA	4234	С	GLN			34.7		54.6		7.728		43.66	6
	MOTA	4235	0	GLN			33.8		54.9		8.397		45.00	8
	ATOM	4236	N	ARG			36.0		55.0		8.113		44.71	7
40	MOTA	4237	CA	ARG			36.2		55.7		9.369		48.39	6
40	ATOM	4238	CB	ARG			37.4		55.1		0.107		51.11	6
	MOTA	4239	CG	ARG			37.3		53.6		10.397		56.82	6
	ATOM	4240	CD	ARG			38.1		53.3		1.641		64.45	6
	MOTA	4241	NE	ARG			37.3		53.6		12.886 13.969		68.42 68.95	7 6
45	MOTA	4242	CZ	ARG			37.9 39.1		54.2 54.6		13.967		66.80	7
40	MOTA	4243		ARG ARG			37.1		54.3		15.907 15.076		69.05	7
	MOTA	4244 4245		ARG			36.3		57.2		9.168		48.49	6
	MOTA	4245	С О	ARG			36.9		57.6		8.161	_	48.13	8
	MOTA MOTA	4247	N	PHE			35.9		57.9		0.133		47.70	7
50	ATOM	4247	CA	PHE			36.0		59.4		10.035		47.31	6
00	ATOM	4249	CB	PHE			34.6		60.0		9.719		43.68	6
	MOTA	4250	CG	PHE			34.0		59.4		8.504		43.63	6
	ATOM	4251		PHE			33.3		58.2		8.549		42.29	6
	ATOM	4252		PHE			34.		60.1		7.301		44.87	6
55	ATOM	4253		PHE			32.3		57.7		37.410		44.63	6
55	MOTA	4254	CE2				33.5		59.6		6.160		45.50	6
	MOTA	4255	CZ	PHE			32.8		58.4		6.213		45.14	6
	ATOM	4256	Ċ	PHE			36.5		60.0		1.280	1.00	46.67	6
	MOTA	4257	ō	PHE			36.5		59.5		12.359		47.10	8
60	MOTA	4258	N	SER			36.9	984	61.3	28 4	11.098	1.00	47.71	7
	MOTA	4259	CA	SER	C 1	22	37.4	<b>1</b> 69	62.1	.50 4	12.187	1.00	49.70	6

							142							
	ATOM	4260	СВ	SER C 1	22		3.799	62.	808	41.8	09	1.00	51.31	6
	ATOM	4261	OG	SER C 1			9.240	63.		42.8			51.16	8
	ATOM	4262	C	SER C 1			5.387	63.		42.3			50.12	6
	ATOM	4263	0.	SER C 1			5.169	64.		41.4			49.00	8
5	ATOM	4264		CYS C 1			5.687	63.		43.4			50.55	7
U	ATOM	4265	CA	CYS C 1			1.636	64.		43.7			52.50	6
	ATOM	4266	C	CYS C 1			4.356	64.		452			54.52	6
	ATOM	4267	0	CYS C 1			4.998	63.		46.0			54.24	8
	MOTA	4268	СВ	CYS C 1			3.377	63.		42.9			53.16	6
10	ATOM	4269	SG	CYS C 1			2.811	62.		43.3			51.95	16
. •	MOTA	4270	N	ASP C 1			3.389	65.		45.6		1.00	56.86	7
	ATOM	4271	CA	ASP C 1			3.047	65.		47.0			58.55	6
	ATOM	4272	CB	ASP C 1			2.265	66.		47.2		1.00	58.22	6
	MOTA	4273	CG	ASP C 1			2.506	67.	105	48.6		1.00	58.91	6
15	ATOM	4274		ASP C 1			2.703	66.		49.5	•	1.00	58.22	8
	MOTA	4275		ASP C 1			2.500	68.		48.7	777	1.00	62.67	8
	MOTA	4276	C	ASP C 1			2.246	64.	055	47.6	501	1.00	58.49	6
	MOTA	4277	Ō	ASP C 1	.24		1.098	63.	837	47.2	229	1.00	58.26	8
	MOTA	4278	N	VAL C 1		3:	2.868	63.	320	48.5	513	1.00	59.01	7
20	ATOM	4279	CA	VAL C 1	.25	3:	2.232	62.	175	49.3	L52	1.00	60.88	6
	MOTA	4280	CB.	VAL C 1	.25	3.	3.224	60.	983	49.2	243	1.00	59.28	6
	MOTA	4281	CG1	VAL C 1	.25	3	2.601	59.	838	49.9	983	1.00	56.75	6
	MOTA	4282	CG2	VAL C 1	25	3	3.639	60.	552	47.8	356	1.00	58.31	6
	MOTA	4283	С	VAL C 1		3	1.740	62.	530	50.	565		63.26	6
25	MOTA	4284	0	VAL C 1		3	0.892	61.	833	51.	143	_	63.90	8
	MOTA	4285	N	SER C 1	L26	3	2.267	63.	616	51.3	122		63.98	7
	MOTA	4286	CA	SER C 1		3	1.878		026	52.4			64.49	6
	MOTA	4287	СВ	SER C 1	126		2.464		400	52.			63.93	6
	MOTA	4288	OG	SER C 1			1.972		381	51.			61.34	8
30	MOTA	4289	С	SER C 1			0.364		061	52.			64.90	6
	MOTA	4290	0	SER C 1			9.654		603	51.			64.08	8
	MOTA	4291	N	GLY C 1			9.871		458	53.			66.05	7
	MOTA	4292	CA	GLY C 1			8.442		458	53.			68.25	6
~=	MOTA	4293	С		L27		7.742		201	53.			69.88	6
35	MOTA	4294	0	GLY C 1			6.546		040	53.			70.57	8
	MOTA	4295	N	VAL C 1			8.480		297	52.			71.23	7
	MOTA	4296	CA	VAL C 1			7.871		065	52.			72.78	6
	MOTA	4297	CB	VAL C 1			8.890		124	51.			72.13 75.47	6 6
40	MOTA	4298		VAL C 1			9.282		670 940	50.5 52.			70.24	6
40	MOTA	4299	C	VAL C 1	128		0.104 7.223		242	53.			74.00	6
	MOTA MOTA	4300 4301	0	VAL C 1			6.090		770	53.			73.73	8
				ASP C 1		_	7.946		063	54.			75.39	7
	MOTA MOTA	4302 4303	N CA	ASP C 1			7.440		222	55.			77.33	6
45	MOTA	4304	CB	ASP C 1			8.490		040	56.			77.51	
70	ATOM	4305	CG	ASP C			8.304		729	57.			78.34	
	MOTA	4306		ASP C 1			9.328		051	57.			78.50	8
	ATOM	4307		ASP C 1			7.132		377	57.			77.23	8
	MOTA	4308	C	ASP C 1			6.114		634	56.			78.98	6
50	ATOM	4309	ō	ASP C			5.497		832	56.		1.00	79.11	
	ATOM	4310	N	THR C			5.645	59.	851	55.	948	1.00	79.48	7
	MOTA	4311	CA	THR C			4.365	60.	250	56.	521	1.00	80.50	6
	MOTA	4312	СВ	THR C 1	130	·2	4.447	60.	229	58.	077		83.19	
	MOTA	4313	OG1	THR C	130	2	5.829	60.	140	58.	472	1.00	82.84	8
55	MOTA	4314	CG2	THR C	130	2	3.618	59.	035	58.	670		83.96	
	MOTA	4315	С	THR C			3.705		566	56.			79.50	
	ATOM	4316	0	THR C			4.362		536	55.			78.71	
	MOTA	4317	N	GLU C			2.382		553	56.			79.39	
^^	MOTA	4318	CA	GLU C :			1.486		700		114		79.61	
60	MOTA	4319	CB	GLU C :			1.981		.893	56.			82.70	
	MOTA	4320	CG	GLU C :	131	. 2	1.680	63.	,772	58.	4/1	T.00	85.13	6

-					-143				
	MOTA	4321	CD G	FLU C 131	22.642	64.580	59.335	1.00 86.47	6
	ATOM	4322		FLU C 131	22.862	65.788	59.024	1.00 87.43	8
	MOTA	4323		GLU C 131	23.168	63.998	60.320	1.00 85.12	8
	MOTA	4324	c c	GLU C 131	21.207	63.185	54.715	1.00 77.86	6
5	MOTA	4325	0 (	GLU C 131	20.460	62.560	53.955	1.00 76.34	8
	MOTA	4326	N S	SER C 132	21.771	64.355	54.428	1.00 76.46	7
	MOTA	4327		SER C 132	21.652	64.995	53.136	1.00 75.54	6
	MOTA	4328		SER C 132	21.941	66.495	53.290	1.00 76.21 1.00 78.77	6 8
	MOTA	4329		SER C 132	23.233	66.719	53.841	1.00 78.77	6
10	MOTA	4330		SER C 132	22.673	64.318	52.205 51.026	1.00 74.56	8
	MOTA	4331		SER C 132	22.799 23.392	64.675 63.338	52.764	1.00 72.74	7
	ATOM	4332		GLY C 133	24.389	62.591	52.704	1.00 70.01	6
	ATOM	4333		GLY C 133' GLY C 133	25.435	63.449	51.337	1.00 68.98	6
15	ATOM	4334		GLY C 133	25.636	64.615	51.686	1.00 69.00	8
15	MOTA	4335 4336		ALA C 134	26.107	62.859	50.355	1.00 66.70	7
	MOTA ATOM	4337		ALA C 134	27.131	63.563	49.609	1.00 64.10	6
	ATOM	4338		ALA C 134	28.394	62.723	49.531	1.00 63.57	6
	ATOM	4339	_	ALA C 134	26.641	63.899	48.212	1.00 62.41	6
20	ATOM	4340		ALA C 134	25.640	63.360	47.737	1.00 60.16	8
	ATOM	4341		THR C 135	27.347	64.826	47.573	1.00 62.33	7
	ATOM	4342		THR C 135	27.023	65.237	46.211	1.00 62.11	6
	MOTA	4343	СВ	THR C 135	26.431	66.642	46.166	1.00 61.79	6
	MOTA	4344		THR C 135	25.253	66.675	46.980	1.00 65.07	8
25	MOTA	4345	CG2	THR C 135	26.057	67.007	44.746	1.00 60.95	6 6
	ATOM	4346	С	THR C 135	28.292	65.181	45.375	1.00 60.85 1.00 61.27	8
	MOTA	4347	0	THR C 135	29.181	66.040	45.473 44.574	1.00 51.27	7
	MOTA	4348	N	CYS C 136	28.368	64.128	44.574	1.00 56.58	6
-	MOTA	4349	CA	CYS C 136	29.499 29.140	63.891 64.393	42.325	1.00 56.26	6
30	MOTA	4350	C	CYS C 136	28.197		41.710	1.00 56.21	8
	MOTA	4351	0	CYS C 136	29.794	62.396	43.698	1.00 54.70	6
	MOTA	4352 4353	CB SG	CYS C 136	31.010	61.882	42.454	1.00 52.66	16
	MOTA MOTA	4353	N	ARG C 137	29.874	65.386	41.843	1.00 55.40	7
35	MOTA	4355	CA	ARG C 137	29.605	65.938	40.520	1.00 55.61	6
00	MOTA	4356	CB	ARG C 137	29.698	67.466	40.537	1.00 56.53	6
	MOTA	4357	CG	ARG C 137	28.713	68.135	41.462	1.00 61.72	6
	MOTA	4358	CD	ARG C 137	29.231	69.491	41.947	1.00 65.19	6
	ATOM	4359	NE	ARG C 137	28.632	69.871	43.236	1.00 69.78	7
40	MOTA	4360	CZ	ARG C 137	27.352	70.221	43.412	1.00 71.88	6
	MOTA	4361		ARG C 137	26.504	70.256	42.384	1.00 74.24	7
	MOTA	4362	NH2	ARG C 137	26.908	70.522	44.626	1.00 70.49 1.00 55.23	7 6
	MOTA	4363	С	ARG C 137	30.604			1.00 57.26	8
	ATOM	4364	0	ARG C 137	31.807	65.381	39.773 38.385		7
45	MOTA	4365	N	ILE C 138	30.095	64.948 64.398			6
	MOTA	4366	CA	ILE C 138 ILE C 138	30.922 30.529				6
	MOTA	4367		ILE C 138	31.361	62.360			6
	MOTA	4368		ILE C 138	30.703	62.090			6
50	MOTA	4369 4370		ILE C 138	30.080	60.706			6
30	ATOM ATOM	4371		ILE C 138	30.693			1.00 48.82	6
	ATOM	4372		ILE C 138	29.571			1.00 46.40	8
	MOTA	4373		LYS C 139	31.752			1.00.49.18	7
•	ATOM	4374		LYS C 139	31.634				6
55	MOTA	4375		LYS C 139	32.364				6
33	ATOM	4376		LYS C 139	31.952				6
	MOTA	4377	CD	LYS C 139	32.477				6
	MOTA	4378		LYS C 139	31.780				6 7
	MOTA	4379		LYS C 139	32.316				6
60		4380		LYS C 139	32.218				8
	MOTA	4381	LO	LYS C 139	33.364	65.446	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	. 1,00 31,04	•

WO 01/58951

-144 31.441 65.761 32.036 1.00 51.29 MOTA 4382 N ILE C 140 31.938 65.091 30.842 CA ILE C 140 1.00 50.15 4383 MOTA 31.404 63.613 31.536 62.955 ILE C 140 30.769 1.00 51.22 4384 CB MOTA ATOM 4385 CG2 ILE C 140 32.134 1.00 52.05 6 29.930 63.555 1.00 49.11 CG1 ILE C 140 30.393 6 MOTA 4386 29.307 62.187 1.00 49.89 30.676 6 CD1 ILE C 140 MOTA 4387 31.624 65.861 1.00 47.99 6 MOTA 4388 ILE C 140 29.560 С 29.365 1.00 50.04 ILE C 140 30.515 66.323 8 MOTA 4389 0 32.620 66.025 1.00 46.57 GLY C 141 28.701 7 MOTA 4390 N GLY C 141 10 32.414 66.732 27.447 1.00 46.87 6 4391 MOTA CA GLY C 141 33.453 66.323 26.416 1.00 46.66 6 MOTA 4392 8 MOTA 4393 ATOM 7 4394 6 **ATOM** 4395 15 б MOTA 4396 8 MOTA 4397 6 MOTA 4398 ATOM 4399 7 4400 N MOTA 20 6 ATOM 4401 4402 6 MOTA 6 MOTA 4403 4404 б MOTA 6 MOTA 4405 25 ATOM 4406 4407 MOTA 7 MOTA 4408 4409 MOTA 6 ATOM 4410 30 6 MOTA 4411 6 ATOM 4412 8 ATOM 4413 7 MOTA 4414 6 MOTA 4415 35 6 MOTA 4416 8 MOTA 4417 б MOTA 4418 MOTA 4419 6 8 MOTA 4420 40 7 MOTA 4421 6 4422 MOTA MOTA 4423 4424 MOTA 6

N GLY C 141 32.620 66.025 28.701 1.00 46.57 CA GLY C 141 32.414 66.732 27.447 1.00 46.68 O GLY C 141 33.453 66.323 26.416 1.00 46.66 O GLY C 141 34.359 65.565 26.739 1.00 46.42 N SER C 142 33.329 66.804 24.10 1.00 41.98 CB SER C 142 33.397 67.165 22.828 1.00 40.96 CB SER C 142 35.662 67.057 21.943 1.00 34.78 CS ER C 142 35.662 67.057 21.943 1.00 34.78 CS ER C 142 35.662 67.057 21.943 1.00 34.78 CS ER C 142 35.662 66.028 24.551 1.00 43.33 O SER C 142 35.662 66.028 24.551 1.00 43.33 O SER C 142 35.915 67.956 25.115 1.00 43.33 O SER C 143 38.025 66.300 24.622 1.00 42.98 CB TRP C 143 38.025 66.300 24.622 1.00 42.98 CB TRP C 143 40.394 65.420 26.820 1.00 36.50 CE2 TRP C 143 40.394 65.625 27.943 1.00 36.50 CE2 TRP C 143 41.795 65.481 26.967 1.00 35.30 CE3 TRP C 143 41.795 65.481 26.967 1.00 36.50 CE2 TRP C 143 42.353 65.625 27.943 1.00 36.55 CD1 TRP C 143 42.353 65.625 27.943 1.00 36.55 CD1 TRP C 143 42.353 65.551 25.738 1.00 35.00 CZ2 TRP C 143 42.353 65.251 25.738 1.00 35.00 CZ2 TRP C 143 42.353 65.551 25.738 1.00 35.00 CZ2 TRP C 143 42.353 65.625 27.943 1.00 36.55 CD1 TRP C 143 42.353 65.251 25.738 1.00 35.00 CZ2 TRP C 143 40.185 65.878 29.153 1.00 35.28 CM2 TRP C 143 39.584 65.625 27.943 1.00 36.50 CZ2 TRP C 143 40.185 65.878 29.153 1.00 35.28 CM2 TRP C 143 39.567 67.915 23.962 1.00 46.65 N THR C 144 38.402 67.065 22.338 1.00 42.21 CA THR C 144 38.402 67.065 22.338 1.00 42.21 CB TRP C 143 39.567 67.915 23.962 1.00 46.65 N THR C 144 38.806 69.611 19.795 1.00 43.02 N HIS C 145 36.695 69.571 19.885 1.00 43.03 CE3 THR C 144 38.890 66.901 20.372 1.00 40.06 CB THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.890 66.963 119.795 1.00 43.03 CE3 THR C 144 38.655 69.571 19.885 1.00 45.42 CB 4425 MOTA 45 7 ATOM 4426 6 MOTA 4427 7 ATOM 4428 6 MOTA 4429 4430 R MOTA 50 7 MOTA 4431 6 MOTA 4432 6 MOTA 4433 6 MOTA 4434 6 MOTA 4435 55 4436 7 ATOM MOTA 4437 35.699 75.043 17.257 1.00 46.12 7 NE2 HIS C 146 MOTA 4438 HIS C 146 33.524 73.188 20.664 1.00 54.19 4439 MOTA C 4440 O HIS C 146 4441 N SER C 147 4442 CA SER C 147 72.531 19.736 1.00 54.21 33.047 MOTA 74.112 21.341 1.00 56.30 7 60 32.847 MOTA 1.00 57.23 6 31.437 74.418 21.115 MOTA

					-145		•		
	ATOM	4443	СВ	SER C 147	31.055	75.610	21.978	1.00 57.36	6
	ATOM	4444		SER C 147	32.017	76.635	21.828	1.00 59.18	8
	ATOM	4445		SER C 147	30.972	74.660	19.682	1.00 57.72	6
	MOTA	4446	0	SER C 147	29.790	74.484	19.375	1.00 57.25	8
5	MOTA	4447	N	ARG C 148	31.885	75.065	18.809	1.00 58.23	7
	MOTA	4448	CA	ARG C 148	31.517	75.336	17.424	1.00 60.12	6
	MOTA	4449	CB	ARG C 148	32.555	76.264	16.777	1.00 63.75	6
	MOTA	4450	CG	ARG C 148	32.799	77.567	17.549	1.00 70.83	6
	MOTA	4451		ARG C 148	33.950	78.393	16.946	1.00 77.31	6
10	MOTA	4452		ARG C 148	34.422	79.453	17.852	1.00 84.18	7 6
	MOTA	4453		ARG C 148	33.696	80.506	18.245	1.00 86.23	7
	MOTA	4454		ARG C 148	32.447	80.661	17.818	1.00 87.64	7
	ATOM	4455		ARG C 148	34.213	81.408	19.072	1.00 86.26 1.00 59.83	6
	ATOM	4456		ARG C 148	31.390	74.051	16.601 15.519	1.00 59.83	8
15	MOTA	4457	0	ARG C 148	30.786	74.053	17.121	1.00 57.69	7
	MOTA	4458	N	GLU C 149	31.954	72.959 71.677	16.425	1.00 54.67	6
	ATOM	4459	CA	GLU C 149	31.937 33.364	71.132	16.321	1.00 52.47	6
	MOTA	4460	CB	GLU C 149	34.395	72.228	16.050	1.00 52.11	6
20	MOTA	4461	CG	GLU C 149 GLU C 149	35.824	71.718	15.896	1.00 50.20	6
20	MOTA	4462 4463	CD OF1	GLU C 149	36.246	70.852	16.678	1.00 49.43	8
	MOTA	4463	OE2	GLU C 149	36.537	72.203	15.004	1.00 47.62	8
	MOTA MOTA	4465	C	GLU C 149	31.043		17.162	1.00 53.64	6
	MOTA	4466	ō	GLU C 149	30.252		16.552	1.00 53.16	8
25	ATOM	4467	N	ILE C 150	31.172	70.667	18.479	1.00 52.16	7
	MOTA	4468	CA	ILE C 150	30.353	69.795	19.289	1.00 51.98	6
	ATOM	4469	CB	ILE C 150	31.157		19.883	1.00 53.49	6
	MOTA	4470	CG2		30.361		21.019	1.00 52.00	6
	MOTA	4471	CG1		31.450		18.800	1.00 53.48	6 6
30	MOTA	4472	CD1	ILE C 150	32.235		19.299	1.00 50.44 1.00 53.26	6
	MOTA	4473	С	ILE C 150	29.750		20.446	1.00 53.20	8
	MOTA	4474	0	ILE C 150			21.095 20.694	1.00 54.99	7
	MOTA	4475	N	SER C 151	28.479 27.749		21.797	1.00 56.94	6
O.E.	ATOM	4476	CA	SER C 151 SER C 151			21.280	1.00 54.85	6
35	ATOM	4477 4478	CB OG	SER C 151			20.557	1.00 55.92	8
	MOTA MOTA	4479	C	SER C 151			22.516	1.00 59.00	6
	ATOM	4480	Ö	SER C 151			21.871	1.00 60.03	8
	MOTA	4481	N	VAL C 152			23.844	1.00 60.32	7
40	ATOM	4482	CA	VAL C 152		68.651	24.655	1.00 61.16	6
	MOTA	4483	СВ	VAL C 152	27.564	68.096	25.694	1.00 60.14	6
	ATOM	4484		. VAL C 152			25.009	1.00 61.98	6
	ATOM	4485	CG2	VAL C 152				1.00 61.23	6
	MOTA	4486	С	VAL C 152			25.391	1.00 62.82	6
45	ATOM	4487		VAL C 152			25.758	1.00 63.73 1.00 65.81	8 7
	MOTA	4488		ASP C 153			25.614	1.00 67.23	6
	MOTA	4489		ASP C 153			26.293 25.249	1.00 67.25	6
	ATOM	4490		ASP C 153			24.320	1.00 72.38	6
<b>E</b> 0	MOTA	4491		ASP C 153 L ASP C 153				1.00 72.90	8
50	MOTA	4492 4493		ASP C 153				1.00 75.01	8
	MOTA MOTA			ASP C 153				1.00 69.10	6
	MOTA	4495		ASP C 153				1.00 68.47	8
	MOTA	4496		PRO C 154				1.00 70.49	7
55	MOTA	4497		PRO C 154		2 69.309			6
-	MOTA	4498		PRO C 154		5 67.098			6
	MOTA	4499	CB	PRO C 154					6
	MOTA	4500		PRO C 154					6
	MOTA	4501		PRO C 154					6 8
60	MOTA	4502		PRO C 154					7
	MOTA	4503	N	THR C 15	. 13.27	J 0J./44	22 .210	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	•

					-146				
	ATOM	4504	CA	THR C 155	18.010	65.253	28.633	1.00 83.84	6
	MOTA	4505	CB	THR C 155	18.244	63.932	27.837	1.00 83.53	6
	MOTA	4506		THR C 155	18.609	62.882	28.744	1.00 83.26	8
	MOTA	4507	CG2	THR C 155	19.361	64.105	26.823	1.00 83.08	6
5	MOTA	4508	С	THR C 155	16.897	65.001	29.678	1.00 87.74	6
	MOTA	4509	0	THR C 155	16.826	65.677	30.715	1.00 87.94	8
	MOTA	4510	N	THR C 156	16.042	64.012	29.370	1.00 91.72	7
	MOTA	4511	CA	THR C 156	14.882	63.577	30.180	1.00 93.73	6
	MOTA	4512	CB	THR C 156	14.501	62.092	29.877	1.00 93.94	6
10	ATOM	4513	OG1		14.249	61.933	28.470	1.00 93.93	8 6
	MOTA	4514	CG2	THR C 156	13.253	61.681	30.696	1.00 93.29 1.00 95.32	6
	MOTA	4515	С	THR C 156	15.042	63.695 62.817	31.693 32.347	1.00 95.61	8
	MOTA	4516	0	THR C 156	15.626 14.490	64.767	32.347	1.00 97.07	7
15	MOTA	4517	N	GLU C 157 GLU C 157	14.578	65.011	33.679	1.00 98.94	6
15	MOTA MOTA	4518 4519	CA CB	GLU C 157	14.487	66.514	33.942	1.00100.27	6
	ATOM	4520	CG	GLU C 157	15.282	67.359	32.950	1.00102.55	6
	ATOM	4521	CD	GLU C 157	15.113	68.852	33.214	1.00104.54	6
	ATOM	4522	OE1		13.943	69.322	33.312	1.00105.88	8
20	ATOM	4523	OE2		16.150	69.555	33.327	1.00104.90	8
	ATOM	4524	Ċ	GLU C 157	13.475	64.290	34.465	1.00 99.30	6
	ATOM	4525	Ö	GLU C 157	13.452	64.337	35.706	1.00 99.77	8
	MOTA	4526	N	ASN C 158	12.557	63.639	33.751	1.00 99.15	7
	MOTA	4527	CA	ASN C 158	11.457	62.919	34.404	1.00 98.32	6
25	MOTA	4528	СВ	ASN C 158	10.382	62.541	33.374	1.00100.43	6
	MOTA	4529	CG	ASN C 158	9.902	63.736	32.555	1.00101.38	6
	MOTA	4530		ASN C 158	9.423	64.738	33.112	1.00101.96	8
	MOTA	4531		ASN C 158	10.026	63.636	31.224	1.00101.40	7
	MOTA	4532	С	ASN C 158	11.991	61.638	35.064	1.00 96.64	6
30	MOTA	4533	0	ASN C 158	12.380	61.643	36.239	1.00 96.33	8 7
	MOTA	4534	N	SER C 159	11.992	60.558	34.283	1.00 93.61 1.00 90.35	6
	ATOM	4535	CA	SER C 159	12.466	59.237 58.788	34.690 33.690	1.00 90.33	6
	ATOM	4536	CB	SER C 159	13.541 14.367	59.898	33.320	1.00 90.44	8
35	ATOM	4537	OG	SER C 159 SER C 159	13.005	59.167	36.123	1.00 88.15	6
33	MOTA MOTA	4538 4539	C O	SER C 159	13.003	59.894	36.481	1.00 88.99	8
	ATOM	4540	N	ASP C 160	12.414	58.302	36.945	1.00 84.53	7
	ATOM	4541	CA	ASP C 160	12.863	58.152	38.330	1.00 80.47	6
	ATOM	4542	CB	ASP C 160	12.232	56.921	38.985	1.00 80.26	6
40	ATOM	4543	CG	ASP C 160	12.760	56.683	40.398	1.00 82.12	6
	ATOM	4544		ASP C 160	12.658	55.536	40.890	1.00 82.78	8
	ATOM	4545		ASP C 160	13.277	57.644	41.023	1.00 82.17	8
	ATOM	4546	С	ASP C 160	14.380	57.978	38.340	1.00 77.39	6
	ATOM	4547	0	ASP C 160	14.892	57.009	37.768	1.00 75.75	8
45	MOTA	4548	N	ASP C 161	15.080	58.910	38.992	1.00 73.66	7
	MOTA	4549	CA	ASP C 161	16.529	58.864	39.072	1.00 71.77	6
	MOTA	. 4550	CB	ASP C 161	17,060	59.934	40.028	1.00 71.93	6
	MOTA	4551	CG	ASP C 161	16.943	61.330	39.461	1.00 72.28	6
	MOTA	4552		ASP C 161	17.115	61.486	38.230	1.00 71.71	8
50	ATOM	4553		ASP C 161	16.695	62.270	40.246	1.00 74.13 1.00 70.97	8
	MOTA	4554	C	ASP C 161	17.118	57.515	39.479 39.222	1.00 70.97	6 8
	MOTA		0	ASP C 161	18.296 16.335	57.251 56.649	40.105	1.00 /3.00	7
	MOTA	4556	N	SER C 162 SER C 162	16.899	55.366	40.103	1.00 66.65	6
55	ATOM	4557 4558	CA CB	SER C 162 SER C 162	17.085	55.308	42.020	1.00 66.09	6
55	MOTA MOTA	4559	OG	SER C 162	15.845	55.352	42.698	1.00 66.84	8
	MOTA	4560		SER C 162	16.064	54.194	40.019	1.00 65.29	6
	ATOM	4561		SER C 162	16.042	53.147	40.646	1.00 65.08	8
	MOTA	4562		GLU C 163	15.393	54.357	38.892	1.00 64.69	7
60	MOTA	4563		GLU C 163	14.571	53.270	38.398	1.00 66.58	б
	MOTA	4564		GLU C 163	13.543	53.784	37.372	1.00 68.86	6

						-147				
	MOTA	4565	CG	GLU C	163	14.029	53.942	35.951	1.00 70.35	6
	ATOM	4566	_	GLU C			54.261	35.000	1.00 73.03	6
	ATOM	4567		GLU C			55.390	35.065	1.00 75.39	8
	ATOM	4568	-		163	12.517	53.378	34.193	1.00 72.63	8
5	ATOM	4569	C	GLU C		15.416	52.145	37.808	1.00 65.46	6
•	ATOM	4570	Ō	GLU C		14.902	51.071	37.481	1.00 64.98	8
	MOTA	4571	N	TYR C		16.718	52.392	37.675	1.00 65.54	7
	ATOM	4572	CA	TYR C		17.647	51.389	37.143	1.00 63.20	6
	ATOM	4573	CB	TYR C		18.353	51.894	35.884	1.00 63.41	6
10	MOTA	4574	CG	TYR C	164	17.433	52.101	34.716	1.00 65.49	6
	MOTA	4575	CD1	TYR C	164	17.299	53.355	34.119	1.00 66.61	6
	MOTA	4576	CE1	TYR C	164	16.429	53.555	33.046	1.00 68.54	6
	MOTA	4577	CD2	TYR C	164	16.676	51.046	34.216	1.00 68.25	6
	MOTA	4578	CE2	TYR C	164	15.797	51.230	33.144	1.00 70.31	6
15	MOTA	4579	CZ	TYR C		15.680	52.484	32.562	1.00 70.26	6
	MOTA	4580	OH	TYR C		14.832	52.655	31.482	1.00 74.21	8
	MOTA	4581	С	TYR C		18.690	51.066	38.184	1.00 61.13	6
	MOTA	4582	0	TYR C		19.480	50.147	38.003	1.00 60.53	8
	MOTA	4583	N	PHE C		18.687	51.824	39.279	1.00 59.92	7
20	MOTA	4584	CA	PHE C		19.657	51.622	40.347	1.00 58.58	6
	MOTA	4585	CB		165	19.497	52.690	41.425	1.00 56.39	6
	MOTA	4586	CG	PHE C		20.717	52.856	42.288	1.00 55.60	6 6
	MOTA	4587		PHE C		21.904	53.336	41.742	1.00 53.27	6
	MOTA	4588		PHE C		20.692	52.497	43.629	1.00 54.20 1.00 53.30	6
25	MOTA	4589		PHE C		23.049	53.451	42.513	1.00 54.70	6
	ATOM	4590		PHE C		21.835	52.607	44.414 43.854	1.00 54.70	6
	MOTA	4591	CZ	PHE C		23.018	53.085 50.250	40.974	1.00 58.64	6
	MOTA	4592	C		165	19.528 18.422	49.749	41.153	1.00 60.35	8
20	ATOM	4593	0	PHE C SER C		20.655	49.631	41.298	1.00 58.50	7
30	MOTA	4594	N CA	SER C		20.614	48.309	41.900	1.00 58.50	6
	MOTA	4595 4596	CB	SER C		22.013	47.703	41.996	1.00 58.83	6
	ATOM ATOM	4597	OG	SER C		21.957	46.391	42.542	1.00 61.34	
	ATOM	4598	C	SER C		20.050	48.473	43.286	1.00 58.49	6
35	MOTA	4599	Ö	SER C		20.346	49.454	43.964	1.00 58.40	8
00	ATOM	4600	N	GLN C		19.249	47.503	43.706	1.00 57.37	· 7
	ATOM	4601	CA	GLN C		18.631	47.545	45.020	1.00 57.17	6
	MOTA	4602	CB	GLN C		17.317	46.766	44.994	1.00 59.70	
	MOTA	4603	CG	GLN C		17.467	45.351	44.490	1.00 62.90	
40	ATOM	4604	CD	GLN C		16.136	44.696	44.164	1.00 67.19	
•	ATOM	4605	OE1	GLN C	167	15.284	44.519	45.048	1.00 68.37	
	MOTA	4606	NE2	GLN C	167	15.940	44.334	42.884	1.00 66.77	
	MOTA	4607	C	GLN C		19.548	46.975	46.085	1.00 55.30	
	MOTA	4608	0	GLN C		19.373	47.235	47.271	1.00 53.36	
45	ATOM	4609	N	TYR C		20.541	46.211	45.659	1.00 55.00	
	MOTA	4610	CA	TYR C		21.455	45.601	46.609	1.00 55.48	
	MOTA	4611	CB	TYR C		21.845	44.214	46.114	1.00 55.25 1.00 56.93	
	MOTA	4612	CG	TYR C		20.630	43.413	45.714	1.00 56.93	
-0	MOTA	4613		TYR C		20.242	43.315	44.378 44.016	1.00 56.50	
50	MOTA	4614		TYR C		19.087	42.640 42.809	46.680	1.00 57.12	
	MOTA	4615		TYR C		19.825 18.664	42.133	46.332	1.00 56.97	
	MOTA	4616	CE2			18.300	42.155	44.997	1.00 58.82	
	MOTA	4617	CZ '	TYR C		17.133	41.408	44.640	1.00 61.29	
55	ATOM	4618 4619	C	TYRC		22.692	46.431	46.919	1.00 55.33	
J	MOTA MOTA	4620	0	TYR C		23.582	45.987	47.637	1.00 53.34	
	MOTA	4621	N	SER C		22.733	47.646	46.384	1.00 56.64	
	ATOM	4622	CA	SER C		23.851	48.553	46.620	1.00 58.03	
	ATOM	4623	CB	SER C		23.731	49.786	45.720	1.00 58.39	
60	MOTA	4624		SER C		24.745	50.727	46.017	1.00 57.3	
<b>-</b>	ATOM	4625		SER C		23.860	49.001	48.076	1.00 60.13	

						-148					
,	MOTA	4626	0 5	SER C	169	22.803	49.148	48.699	1.00 6		8
	ATOM	4627		ARG C		25.052	49.215	48.621	1.00 5		7
	ATOM	4628		ARG C		25.174	49.662	49.998	1.00 5		6
	MOTA	4629		ARG C		26.636	49.602	50.438	1.00 5		6
5	ATOM	4630		ARG C		26.999	48.350	51.195	1.00 6		6
•	ATOM	4631		ARG C		28.466	47.972	51.024	1.00 6	4.86	· 6
	ATOM	4632		ARG C		29.418	49.012	51.424	1.00 6		7
	ATOM	4633		ARG C		30.317	49.556	50.597	1.00 6		6
	ATOM	4634		ARG C		30.384	49.165	49.326	1.00 6		7
10	ATOM	4635		ARG C		31.166	50.480	51.039	1.00 6		7
. •	ATOM	4636		ARG C		24.668	51.102	50.109	1.00 5		6
	MOTA	4637		ARG C		24.416		51.215	1.00		8
	MOTA	4638	N	PHE C	171	24.498		48.968	1.00		7
	ATOM	4639	CA	PHE C	171	24.063		48.982	1.00		6
15	MOTA	4640	CB	PHE C	171	25.131		48.324	1.00		6
. •	ATOM	4641	CG	PHE C	171	26.521		48.814	1.00		6
	MOTA	4642	CD1	PHE C	171	27.189		48.400	1.00		6
		4643		PHE C		27.145		49.724	1.00		6
	MOTA	4644	CE1	PHE C	171	28.463		48.890	1.00		6
20	MOTA	4645		PHE C		28.412		50.218	1.00		6
	MOTA	4646		PHE C		29.074		49.799	1.00		6
	MOTA	4647		PHE C		22.732			1.00		6
	MOTA	4648		PHE C		22.164		47.761	1.00		8
	MOTA	4649		GLU C		22.228		48.376	1.00		7 6
25	MOTA	4650		GLU C		20.947		47.760	1.00 1.00		6
	MOTA	4651	CB	GLU C		19.806		48.789	1.00		6
	MOTA	4652	CG	GLU C		19.891		49.981			6
	MOTA	4653	CD	GLU C		18.753		50.992	1.00	65.38	8
	MOTA	4654		GLU C		17.626		50.557		64.87	8
30	MOTA	4655		GLU C		18.976		52.216 47.162		59.71	6
	MOTA	4656	C	GLU C		21.01		47.102		60.04	8
	MOTA	4657	0	Gru C		21.81		46.154		58.96	7
	MOTA	4658	N	ILE C		20.186 20.18		45.494		59.79	6
0.5	MOTA	4659	CA	ILE C		20.10		43.970		60.17	6
35	MOTA	4660	CB	ILE C		19.91		43.334		57.73	6
	MOTA	4661	CG2	ILE C		21.19		43.384		59.23	6
	MOTA	4662		ILE C		21.05		41.902		58.26	6
	ATOM	4663		ILE C		19.08		45.977		59.99	6
40	MOTA	4664	C	ILE C		17.91				57.81	8
40	MOTA	4665 4666	N O	LEU C		19.48				60.93	7
	MOTA	4667	CA	LEU C		18.51		46.782		62.65	6
	MOTA ATOM	4668	CB	LEU (		19.16				62.58	6
	ATOM	4669	CG	LEU (		19.96				63.64	6
45	ATOM	4670		LEU (		20.64				63.25	6
70	MOTA	4671		LEU (		19.05				61.62	6
	ATOM	4672	c	LEU (		17.98	5 61.680	45.564		64.25	6
	ATOM	4673	ŏ		174	16.78		45.329		65.71	8
	ATOM	4674			175	18.89	3 62.223	44.768		65.23	7
50	MOTA	4675			175	18.48	5 62.951			66.02	6
•	MOTA	4676			175	17.94	9 64.334			67.24	6
	MOTA	4677			175	17.41				68.54	6
	MOTA	4678	OD1	ASP	C 175	16.59				69.53	8
	MOTA	4679	OD2	ASP	C 175	17.81				66.59	8
55	MOTA	4680	С		C 175	19.65				66.29	6
-	MOTA	4681			C 175	20.82				66.20	8
	MOTA	4682			C 176		2 63 237			66.07	7
	MOTA	4683			C 176	20.30				65.83	6
	MOTA	4684			C 176	20.42				66.59	6 6
60	MOTA	4685		VAL	C 176	21.38				64.35 63.70	6
	MOTA	4686	CG2	VAL	C 1/6	20.90	0 60.943	, +0.404	2.00	55.75	v

	W O 01/5	0731						PC 1/EFV1/VI	437
					-149	•			
	7.000	4687	С	VAL C 176	19.869	64.532	39.368	1.00 67.12	6
	ATOM	4688	0	VAL C 176	18.715	64.589	38.956	1.00 67.64	8
	MOTA MOTA	4689	N	THR C 177	20.786	65.447	39.075	1.00 68.63	7
	ATOM	4690	CA	THR C 177	20.482	66.573	38.200	1.00 69.48	6
5	MOTA	4691	CB	THR C 177	20.215	67.861	39.004	1.00 69.26	6
•	ATOM	4692	OG1		21.310	68,.109	39.894	1.00 68.92	8
	ATOM	4693	CG2		18.932	67.718	39.804	1.00 68.40	6
	ATOM	4694	C	THR C 177	21.640	66.813	37.245	1.00 70.44	6 8
	MOTA	4695	0	THR C 177	22.802	66.641	37.614	1.00 69.76	7
10	MOTA	4696	N	GLN C 178	21.312	67.207	36.018	1.00 71.94 1.00 73.43	6
	MOTA	4697	CA	GLN C 178	22.320	67.470	34.998	1.00 75.43	6
	MOTA	4698	CB	GLN C 178	22.150	66.500	33.831	1.00 70.20	6
	MOTA	4699	CG	GLN C 178	21.560	65.148 64.046	34.220 33.196	1.00 83.21	6
	MOTA	4700		GLN C 178	21.896	64.237	31.973	1.00 84.40	8
15	MOTA	4701	OE1		21,745 22.346	62.889	33.694	1.00 82.90	7
	MOTA	4702		GLN C 178	22.346	68.884	34.482	1.00 72.16	6
	MOTA	4703	С	GLN C 178	21.070	69.244	34.044	1.00 72.49	8
	MOTA	4704	0	GLN C 178 LYS C 179	23.214	69.675	34.522	1.00 71.74	7
00	MOTA	47.05	N CA	LYS C 179	23.166	71.054	34.048	1.00 71.38	6
20	MOTA	4706 4707	CB	LYS C 179	23.205	72.022	35.233	1.00 73.17	6
	ATOM	4707	CG	LYS C 179	22.291	71.610	36.380	1.00 78.41	6
	MOTA MOTA	4709	CD	LYS C 179	22.499	72.459	37.644	1.00 79.07	6
	ATOM	4710	CE	LYS C 179	21.814	71.821	38.864	1.00 80.35	6
25	ATOM	4711	NZ	LYS C 179	22.363	70.452	39.163	1.00 81.10	7
	ATOM	4712	С	LYS C 179	24.384	71.301	33.176	1.00 70.13	6
	MOTA	4713	0	LYS C 179	25.504	71.353	33.681	1.00 70.65	8
	MOTA	4714	N	LYS C 180	24.180	71.466	31.876	1.00 68.21	7 6
	MOTA	4715	CA	LYS C 180	25.306	71.719	30.978	1.00 67.25	6
30	MOTA	4716	CB	LÝS C 180	24.833	71.667	29.519	1.00 67.12 1.00 63.90	6
	MOTA	4717	· CG	LYS C 180	24.008	72.846	29.053	1.00 63.70	6
	MOTA	4718	CD	LYS C 180	24.908	73.920	28.488 27.223	1.00 63.70	6
	MOTA	4719	CE	LYS C 180	25.645	73.452	26.013	1.00 62.80	7
	MOTA	4720	NZ	LYS C 180	24.768 25.971	73.295 73.075	31.266	1.00 67.33	6
35	MOTA	4721	C	LYS C 180	25.552	73.803	32.160	1.00 66.68	8
	ATOM	4722	0	LYS C 180 ASN C 181	27.027	73.399	30.528	1.00 67.89	7
	MOTA	4723	N		27.698	74.674	30.702	1.00 67.78	6
	ATOM	4724	CA CB		27.967	74.948	32.191	1.00 69.90	6
40	MOTA	4725 4726	CG		28.580	73.770	32.916	1.00 70.82	6
40	MOTA MOTA	4727		1 ASN C 181	29.508	73.137	32.422	1.00 73.77	8
	ATOM	4728			28.071	73.481	34.109	1.00 70.00	7
	MOTA	4729		ASN C 181	28.977		29.901	1.00 67.29	6
	MOTA	4730		ASN C 181	29.937		30.049		8
45	MOTA	4731		SER C 182	28.978		29.058		7
	MOTA	4732		SER C 182	30.134		28.233	1.00 66.28	6
	MOTA	4733			29.726		27.186		6
	MOTA	4734			30.731		26.214		· 8
	ATOM	4735	C	SER C 182	31.230				8
50	MOTA	4736	0	SER C 182	30.941		_		7
	ATOM	4737	N	VAL C 183	32.483				6.
	MOTA	4738			33.613				6
	MOTA	4739			.33.872				6
	MOTA	4740		31 VAL C 183	33.648				6
, 55		474		32 VAL C 183	35.292 34.925				6
	MOTA	4742		VAL C 183 VAL C 183	35.30				8
	MOTA				35.616				7
	MOTA				36.89				6
60	MOTA				36.99			2 1.00 67.80	6
90	MOTA MOTA			G1 THR C 184	35.98				8
	T TOTA								

					150 :				
					-150 ·	00 406	27.094	1.00 66.48	6
	ATOM	4748		THR C 184	38.370 38.032	80.406 78.470	29.292	1.00 70.57	6
	MOTA	4749		THR C 184 THR C 184	37.920	78.802	30.482	1.00 70.99	8
	ATOM ATOM	4750 4751		TYR C 185	39.118	77.869	28.815	1.00 70.74	7
5	MOTA	4752		TYR C 185	40.236	77.572	29.683	1.00 71.98	6
Ū	MOTA	4753	СВ	TYR C 185	40.555	76.067	29.658	1.00 72.58	` 6
	ATOM	4754	CG	TYR C 185	39.351	75.195	29.937	1.00 72.59	6
	ATOM	4755		TYR C 185	38.363	75.011	28.970	1.00 73.55	6
	MOTA	4756		TYR C 185	37.224	74.258	29.236	1.00 72.54	6 6
10	MOTA	4757		TYR C 185	39.164	74.597	31.185	1.00 72.27 1.00 71.72	6
	ATOM	4758	CE2	TYR C 185	38.017 37.057	73.839 73.678	31.461 30.480	1.00 71.72	6
	MOTA	4759	CZ	TYR C 185 TYR C 185	35.920	72.951	30.732	1.00 71.36	8
	ATOM ATOM	4760 4761	OH C	TYR C 185	41.426	78.355	29.191	1.00 73.72	6
15	ATOM	4762	0	TYR C 185	41.625	78.492	27.983	1.00 74.41	8
10	MOTA	4763	N	SER C 186	42.220	78.869	30.125	1.00 75.63	7
	MOTA	4764	CA	SER C 186	43.405	79.653	29.772	1.00 77.64	6
	MOTA	4765	CB	SER C 186	44.183	80.015	31.043	1.00 77.47	6
	MOTA	4766	OG	SER C 186	44.398	78.870	31.858	1.00 78.93	8 6
20	MOTA	4767	С	SER C 186	44.300	78.875	28.793 27.893	1.00 77.75 1.00 76.44	8
	MOTA	4768	0	SER C 186	44.926 44.332	79.457 77.556	28.977	1.00 78.65	7
	MOTA	·4769	N	CYS C 187 CYS C 187	45.116	76.648	28.135	1.00 79.38	6
	MOTA MOTA	4770 4771	CA C	CYS C 187	44.658	76.703	26.715	1.00 79.55	6
25	MOTA	4772	Ö	CYS C 187	45.443	76.687	25.771	1.00 79.09	8
	ATOM	4773	CB	CYS C 187	44.899	75.178	28.529	1.00 79.04	6
	MOTA	4774	SG	CYS C 187	43.205	74.462	28.241	1.00 80.14	16
	MOTA	4775	N	CYS C 188	43.345	76.774	26.589	1.00 80.45	7
	MOTA	4776	CA	CYS C 188	42.727	76.642	25.305	1.00 79.63 1.00 79.24	6 6
30	MOTA	4777	C	CYS C 188	41.779	77.755	24.835 25.504	1.00 75.24	8
	MOTA	4778	0	CYS C 188 CYS C 188	40.785 42.037	78.065 75.269	25.365	1.00 79.66	6
	MOTA	4779 4780	CB SG	CYS C 188	42.984	73.203	26.264	1.00 75.61	16
	MOTA MOTA	4781	N	PRO C 189	42.070	78.346	23.656	1.00 77.55	7
35	MOTA	4782	CD	PRO C 189	43.222	77.849	22.879	1.00 76.91	6
	ATOM	4783	CA	PRO C 189	41.378	79.431	22.922	1.00 75.67	6
	MOTA	4784	CB	PRO C 189	41.921	79.283	21.502	1.00 75.82	6
	MOTA	4785	CG	PRO C 189	43.328	78.858	21.747	1.00 77.27	6 6
	MOTA	4786	С	PRO C 189	39.835	79.468	22.927 23.459	1.00 73.97	8
40	MOTA	4787	0	PRO C 189	39.233 39.201	80.403 78.465	22.317	1.00 71.85	7
	MOTA	4788 4789	N CA	GLU C 190 GLU C 190	37.734	78.404	22.246	1.00 68.61	6
	ATOM ATOM	4790	CB	GLU C 190	37.305	77.497	21.099	1.00 70.45	6
	MOTA	4791	CG	GLU C 190	38.277	77.434	19.945	1.00 72.05	6
45	MOTA	4792	CD	GLU C 190	38.082	78.554	18.969	1.00 73.59	6
	ATOM	4793		GLU C 190	36.908	78.876	18.657	1.00 73.46	8
	MOTA	4794		2 GLU C 190	39.106	79.100	18.504	1.00 77.52	8 6
	MOTA	4795		GLU C 190	37.084	77.889	23.528 24.501	1.00 64.48 1.00 64.47	8
E0.	MOTA	4796		GLU C 190	37.762 35.764	77.596 77.765	23.514	1.00 60.72	7
50	MOTA	4797 4798		ALA C 191 ALA C 191	35.035	77.281	24.679	1.00 60.54	6
	MOTA MOTA	4799		ALA C 191	33.755	78.075	24.854	1.00 59.52	6
	MOTA	4800		ALA C 191	34.702	75.796		1.00 60.66	6
	ATOM	4801		ALA C 191	34.423	75.306	23.458		8
55	MOTA	4802		TYR C 192	34.717				7
	MOTA	4803			34.409				6
	MOTA	4804			35.621				6 6
	ATOM	4805			36.737 37.694				6
60	MOTA	4806		1 TYR C 192 1 TYR C 192	38.680				6
00	MOTA MOTA	4807 4808		2 TYR C 192	36.800				6

							•			
						-151				_
	MOTA	4809	CE2 T	YR C 192	2	37.785	71.874	23.121	1.00 57.49	6
	ATOM	4810		YR C 192		38.720	72.898	23.119	1.00 58.13	6
	ATOM	4811		YR C 19		39.689	72.918	22.148	1.00 58.55	8
		4812		YR C 19		33.204	73.295	26.508	1.00 57.26	6
5	MOTA	4813		YR C 19		33.292	73.241	27.736	1.00 57.40	8
5	MOTA			LU C 19		32.084	73.042	25.836	1.00 57.28	· <b>7</b>
	ATOM	4814		LU C 19		30.839	72.678	26.506	1.00 58.77	6
	ATOM	4815				29.681	72.597	25.495	1.00 59.02	6
	MOTA	4816		LU C 19		29.342	73.912	24.823	1.00 61.64	6
40	MOTA	4817		LU C 19		28.118	73.827	23.945	1.00 63.79	6
10	MOTA	4818		LU C 19		27.107	73.242	24.411	1.00 66.05	8
	MOTA	4819		LU C 19			74.355	22.805	1.00 63.82	8
	MOTA	4820		LU C 19		28.171	71.336	27.224	1.00 58.56	6
	MOŢA	4821		LU C 19		30.968		26.811	1.00 58.35	8
	MOTA	4822		LU C 19		31.749	70.471	28.296	1.00 57.04	7
15	MOTA	4823		ASP C 19		30.197	71.171	29.059	1.00 57.30	6
	MOTA	4824		ASP C 19		30.215	69.940		1.00 57.30	6
	MOTA	4825		ASP C 19		31.473	69.849	29.932	1.00 58.91	6
	MOTA	4826		ASP C 19		31.430	70.777	31.141		8
	MOTA	4827		ASP C 19		32.220	71.742	31.172	1.00 57.40	8
20	MOTA	4828	OD2 I	ASP C 19	94	30.614	70.538	32.060	1.00 58.46	6
	MOTA	4829		ASP C 19		28.982	69.848	29.933	1.00 56.78	
	MOTA	4830	0 2	ASP C 19	94	28.411	70.864	30.320	1.00 56.90	8
	MOTA	4831	N A	VAL C 19	95	28.567	68.619	30.223	1.00 55.47	7
	MOTA	4832	CA '	VAL C 19	95	27.404	68.373	31.061	1.00 55.52	6.
25	MOTA	4833	CB '	VAL C 19	95	26.538	67.236	30.504	1.00 54.50	6
	ATOM	4834	CG1	VAL C 19	95	25.469	66.841	31.511	1.00 52.44	6
	MOTA	4835		VAL C 1		25.914	67.671	29.199	1.00 55.96	6
	MOTA	4836		VAL C 1		27.874	67.973	32.444	1.00 56.12	6
	ATOM	4837		VAL C 1		28.661	67.046	32.602	1.00 56.74	8
30	ATOM	4838		GLU C 1		27.388	68.675	33.451	1.00 56.91	7
. 00	ATOM	4839		GLU C 1		27.777	68.370	34.816	1.00 57.46	6
	MOTA	4840		GLU C 1		28.051	69.654	35.581	1.00 58.09	6
	MOTA	4841		GLU C 1		28.548	69.445	36.972	1.00 59.59	6
	MOTA	4842		GLU C 1		28.730	70.758	37.700	1.00 62.33	6
35		4843		GLU C 1		29.523	71.594	37.229	1.00 62.53	8
55	MOTA	4844		GLU C 1		28.074	70.958	38.746	1.00 65.85	8
	MOTA	4845		GLU C 1		26.636	67.627	35.453	1.00 57.05	6
	MOTA	4846		GLU C 1		25.517	68.120	35.487	1.00 59.06	8
	MOTA	4847		VAL C 1		26.914	66.427	35.938	1.00 56.46	7
40	MOTA	4848		VAL C 1		25.889	65.612	36.566	1.00 55.58	6
40	MOTA	4849		VAL C 1		25.867	64.179	35.984	1.00 53.38	6
	MOTA			VAL C 1		24.777	63.360	36.649	1.00 50.20	6
	MOTA	4850	CGT	VAL C 1	.57 97	25.629		34.486	1.00 51.56	6
	ATOM	4851		VAL C 1	97	26.199		38.041	1.00 56.50	6
45	MOTA	4852		VAL C 1		27.320			1.00 58.31	8
45	MOTA	4853		SER C 1		25.214		38.866		7
	MOTA	4854				25.407				6
	MOTA	4855		SER C 1	100	24.867				6
	MOTA	4856		SER C		25.661				8
	MOTA	4857		SER C		24.717				6
50	MOTA	4858		SER C	100	23.513				8
	MOTA	4859		SER C						7
	MOTA	4860		LEU C		25.494				6
	MOTA	4863		LEU C		24.938				6
	MOTA	4862		LEU C		25.824			_	6
55		486	3 CG	LEU C		25.457			_	
	MOTA	486		LEU C	T 3 3	24.073				
	MOTA			LEU C		26.487				
	MOTA	486		LEU C		24.818				
	MOTA			LEU C		25.819				
60				ASN C		23.593	_			
	MOTA	486	9 CA	ASN C	200	23.35	, 05.100	, 43,40.		=

							-152					
	ATOM	4870	СВ	ASN (	С	200	22.285	64.232	45.754		60.17	6
	ATOM	4871		ASN (			21.985	64.387	47.239	1.00	62.50	6
	ATOM	4872		ASN			22.905	64.419	48.070		64.15	8
	MOTA	4873		ASN (			20.700	64.480	47.583	1.00	61.21	7
5 -	MOTA	4874	С	ASN (	С	200	22.898	61.801	45.988		55.97	_. 6
	ATOM	4875	0	ASN	С	200	21.821	61.316	45.627	1.00	54.75	8
	MOTA	4876	N	PHE	С	201	23.739	61.181	46.802	1.00	53.51	7
	MOTA	4877	CA	PHE	С	201	23.454	59.867	47.330		53.54	6
	MOTA	4878	CB	PHE	С	201	24.169	58.807	46.503	1.00	50.74	6
10	MOTA	4879	CG	PHE	С	201	25.663	58.820	46.677		48.36	6
	ATOM	4880		PHE			26.312	57.763	47.309		45.72	6
	MOTA	4881		PHE			26.413	59.912	46.252		46.85	6
	MOTA	4882	CE1	PHE	С	201	27.689	57.794	47.521		43.95	6
	MOTA	4883	CE2	PHE			27.782	59.955	46.457		45.93	6
15	MOTA	4884	CZ	PHE			28.425	58.889	47.096		44.09	6
	MOTA	4885	С	PHE			23,979	59.812	48.749		55.36	6
	MOTA	4886	0	PHE			24.640	60.739	49.210		53.66	8
	MOTA	4887	N	ARG			23.698	58.702	49.425		57.35	7
	MOTA	4888	CA	ARG			24.140	58.511	50.792		59.95	6
20	MOTA	4889	CB	ARG			23.192	59.224	51.744		62.36	6
	MOTA	4890	CG	ARG			21.844	58.529	51.789		64.26	6
	MOTA	4891	CD	ARG			20.831	59.278	52.610		67.26	6
	MOTA	4892	NE	ARG			19.555	58.567	52.620		70.54	7
	MOTA	4893	CZ	ARG			18.430	59.062	53.129		69.46	6 7
25	MOTA	4894		ARG			18.420	60.270	53.670		69.25 69.56	7
	MOTA	4895		ARG			17.315	58.349	53.095		60.80	6
	MOTA	4896	C	ARG			24.116	57.023	51.119 50.445		60.45	8
	MOTA	4897	0	ARG			23.439 24.860	56.231 56.651	52.158		61.42	7
30	MOTA	4898	N	LYS LYS			24.886	55.270	52.603		60.82	6
30	MOTA	4899 4900	CA CB	LYS			25.931	55.088	53.703		59.66	6
	MOTA	4901	CG	LYS			25.988	53.688	54.258		61.19	6
	ATOM ATOM	4902	CD	LYS			26.955	53.617	55,404		63.27	6
	ATOM	4903	CE	LYS			27.036	52.209	55.947		66.98	6
35	ATOM	4904	NZ	LYS			27.621	51.250	54.945		68.80	7
-	ATOM	4905	C	LYS			23.477	55.037	53.157		60.81	6
	MOTA	4906	ō	LYS			22.878	55.942	53.735	1.00	60.52	8
	ATOM	4907	N	LYS			22.913	53.858	52.944	1.00	60.36	7
	ATOM	4908	CA	LYS			21.584	53.606	53.466	1.00	60.22	6
40	MOTA	4909	CB	LYS			21.017	52.329	52.837	1.00	58.64	6
	MOTA	4910	CG	LYS	С	204	20.591	52.487	51.381	1.00	55.82	6
	MOTA	4911	CD	LYS	С	204	20.445	51.140	50.692		51.95	6
	MOTA	4912	CE	LYS	С	204	19.975	51.298	49.253		52.70	6
	MOTA	4913	NZ	LYS	С	204	19.967	50.027	48.458		51.76	7
45	MOTA	4914	С	LYS	С	204	21.742	53.460	54.977		62.01	6
	MOTA	4915	0	LYS			22.711	52.854	55.440		63.36	8
	MOTA	4916	N	GLY			20.811	54.022	55.747		62.55	7
	ATOM	4917		. GLY			20.898	53.921	57.202		62.30	6
	MOTA	4918	C	GLY			19.797	53.078	57.844		61.75	6
50	MOTA	4919		GLY			18.911	52.614	57.093		60.18	8
	MOTA	4920		GLY			19.811	52.879	59.092		60.86	8
	MOTA	4921	CB	PHE		1	39.182	71.754	1.648		71.47 73.60	6 6
	MOTA	4922	CG	PHE		1	40.239	71.385 70.241	0.623		75.22	
E E	MOTA	4923		PHE		1	40.122	70.241	-0.169 0.493		73.83	. 6 6
55	MOTA	4924		PHE		1 1	41.397 41.141	69.886	~1.081		75.00	6
	MOTA	4925		PHE PHE		1	42.418	71.835	-0.410		73.00	6
	MOTA	4926	CEZ	PHE		1	42.289	70.688	-1.199		74.63	6
	ATOM ATOM	4927 4928	C	PHE		1	37.071	70.999	2.658		68.35	6
60	ATOM	4929	0	PHE		1	37.607	71.392	3.688		69.33	8
	MOTA	4930	N	PHE		ī	37.010	72.284	0.515		69.08	7
	0.1				_	_	- · · · - <del>- ·</del>				_	

WO 01/58951

-153 1.321 1.00 69.54 6 37.756 71.268 MOTA 4931 CA PHE D 1 2.678 1.00 67.84 7 70.338 35.915 2 MOTA 4932 N ASP D 6 3.967 1.00 66.03 70.061 ASP D 35.253 2 4933 MOTA CA 3.772 1.00 66.47 6 69.266 33.949 ASP D 2 4934 CB MOTA 2.928 1.00 68.89 6 68.032 34.138 CG ASP D 2 5 4935 MOTA 8 3.287 1.00 68.16 67.218 35.029 OD1 ASP D 2 4936 MOTA 8 1.912 1.00 70.47 33.396 67.886 OD2 ASP D 2 4937 MOTA 4.933 1.00 64.63 6 69.310 36.181 MOTA 4938 С ASP D 2 4.672 1.00 64.43 8 37.378 69.165 MOTA 4939 0 ASP D 2 7 6.049 1.00 62.26 35.639 68.837 10 ARG D 3 MOTA 4940 N 7.029 1.00 60.44 6 36.461 68.128 3 ARG D MOTA 4941 CA 8.388 1.00 60.90 6 35.748 68.078 ARG D 3 4942 MOTA CB 36.068 69.254 9.302 1.00 60.80 6 3 4943 ARG D MOTA CG 6 35.185 69.243 10.532 1.00 65.18 ARG D 3 4944 MOTA CD 7 1.00 66.90 35.849 69.838 11.696 15 4945 ARG D 3 NE MOTA 1.00 66.63 6 36.028 71.141 11.888 ARG D 3 4946 CZMOTA 1.00 68.16 7 35.591 72.031 11.002 MOTA 4947 NH1 ARG D 3 12.964 1.00 66.33 36.664 71.553 36.831 66.719 37.938 66.252 7 NH2 ARG D 3 4948 MOTA 6 1.00 59.10 6.580 ARG D 3 4949 С MOTA 6.845 1.00 57.28 8 ARG D 3 20 4950 MOTA 0 7 35.909 66.050 1.00 56.67 5.891 ALA D 4 ATOM 4951 N 6 5.414 1.00 53.48 36.153 64.699 ALA D 4 4952 CA MOTA 34.938 64.175 1.00 52.26 6 4.706 4 4953 CB ALA D ATOM 1.00 53.39 6 37.347 64.696 4.479 4954 C ALA D 4 MOTA 1.00 52.40 8 38.225 63.851 4.600 25 4955 ALA D 4 MOTA 0 1.00 54.53 7 37.381 65.650 3.550 5 ASP D 4956 N MOTA 1.00 55.71 6 2,602 38.489 65.756 ASP D 5 4957 CA MOTA 1.00 58.22 1.627 6 38.266 66.914 ASP D 5 MOTA 4958 CB 1.00 61.46 6 0.881 ASP D 36.938 66.810 5 4959 CG MOTA 1.00 64.32 36.605 65.709 0.386 8 5 30 4960 OD1 ASP D MOTA 0.773 1.00 63.22 8 36.227 67.832 4961 OD2 ASP D 5 MOTA 1.00 54.28 6 39.816 65.970 3.326 ASP D 5 MOTA 4962 C 2.914 1.00 52.86 40.844 65.440 5 4963 ASP D MOTA 0 1.00 52.53 4.410 66.735 39.787 ILE D 6 4964 MOTA N 5.154 1.00 53.69 6 41.007 67.003 ILE D 35 MOTA 4965 CA 6.191 1.00 55.79 6 68.128 40.813 ILE D 6 CB MOTA 4966 1.00 54.61 6 6.877 68.435 CG2 ILE D 42.152 6 4967 MOTA 1.00 55.83 6 5.499 69.385 40.266 4968 CG1 ILE D 6 MOTA 1.00 55.01 6 70.597 6.400 40.121 . 6 MOTA 4969 CD1 ILE D 5.870 1.00 52.43 6 41.545 65.775 40 ILE D 6 4970 С MOTA 1.00 52.78 8 42.711 65.420 5.709 ILE D 6 MOTA 4971 0 6.666 1.00 51.01 7 40.701 65.134 7 4972 N LEU D MOTA 6 1.00 50.01 7.401 41.111 63.949 LEU D 7 ATOM 4973 CA 1.00 47.85 б 8.276 39.962 63.459 LEU D 7 MOTA 4974 CB 1.00 46.02 6 9.408 39.608 64.420 LEU D 7 45 MOTA 4975 CG 1.00 48.59 38.267 64.084 10.010 6 7 4976 CD1 LEU D MOTA 1.00 45.91 6 40.687 64.356 10.440 CD2 LEU D 7 4977 MOTA 1.00 51.80 6 41.526 62.871 6.415 7 TEA. D 4978 С MOTA 1.00 52.35 42.507 62.154 6.631 7 LEU D 4979 0 MOTA 1.00 52.55 7 5.315 40.788 62.781 8 TYR D 50 MOTA 4980 N 1.00 53.16 б 61.788 4.288 41.060 8 TYR D MOTA 4981 CA 1.00 54.45 6 40.047 61.936 3.159 TYR D 8 MOTA 4982 CB 61.006 2.006 1.00 57.19 6 40.294 CG 8 4983 TYR D ATOM 1.00 57.12 6 40.030 59.646 2.120 CD1 TYR D 8 4984 MOTA 1.00 60.62 6 1.069 58.772 8 40.308 55 CE1 TYR D 4985 MOTA 1.00 58.57 61.481 0.810 6 40.841 Я 4986 CD2 TYR D MOTA -0.247 1.00 60.35 6 41.130 60.617 CE2 TYR D 8 MOTA 4987 -0.112 1.00 61.47 6 40.863 59.264 TYR D ATOM 4988 CZ1.00 62.53 8 41.162 58.403 -1.149 TYR D 8 OH MOTA 4989 42.483 1.00 53.38 61.905 3.735 6 TYR D 8 60 4990 С MOTA 1.00 53.74 43.190 60.907 3.591 TYR D 8 4991 0 MOTA

							-154				
	ATOM	4992	N	ASN D	9		42.900	63.121	3.416	1.00 53.53	7
	ATOM	4993		ASN D			44.238	63.329	2.890	1.00 55.79	6
	ATOM	4994		ASN D	9		44.451	64.800	2.509	1.00 59.06	6
	MOTA	4995	CG	ASN D	9		43.588	65.232	1.317	1.00 63.96	6
5	MOTA	4996	OD1	ASN D	9		42.912	64.406	0.688	1.00 67.47	. 8
	ATOM	4997	ND2	ASN D	9		43.612	66.527	1.000	1.00 65.39	7
	ATOM	4998	С	ASN D	9		45.283	62.901	3.907	1.00 55.13	6
	MOTA	4999	0	ASN D	) 9		46.175	62.117	3.593	1.00 54.15	8
	MOTA	5000	N	ILE D			45.167	63.416	5.129	1.00 55.13	7
10	MOTA	5001	CA	ILE D			46.099	63.077	6.195	1.00 54.61	6 6
	MOTA	5002	CB	ILE D			45.660	63.693	7.534	1.00 54.44 1.00 53.71	6
	MOTA	5003		ILE D			46.585	63.218	8.651	1.00 53.71	6
	MOTA	5004	_	ILE I			45.683	65.222	7.435	1.00 32.93	6
	MOTA	5005		ILE I			45.083	65.916 61.566	8.605 6.365	1.00 47.32	6
15	MOTA	5006	С	ILE I			46.177	60.992	6.496	1.00 57.11	8
	ATOM	5007	0	ILE I			47.258	60.927	6.363	1.00 56.48	7
	MOTA	5008	N	ARG I			45.018 44.938	59.494	6.512	1.00 58.41	6
	ATOM	5009	CA	ARG I			44.938	59.070	6.428	1.00 63.58	6
00	MOTA	5010	CB	ARG I			43.229	57.585	6.631	1.00 70.33	6
20	MOTA	5011	CD	ARG I	_		43.398	57.219	8.100	1.00 79.03	6
	MOTA	5012 5013	NE	ARG I			42.703	55.980	8.448	1.00 85.37	7
	ATOM ATOM	5013	CZ	ARG I			41.466	55.685	8.037	1.00 88.61	6
	MOTA	5015		ARG I			40.795	56.548	7.249	1.00 89.11	7
25	ATOM	5016		ARG I			40.890	54.545	8.434	1.00 87.93	7
	MOTA	5017	C	ARG			45.721	58.778	5.425	1.00 58.93	6
	MOTA	5018	Ō	ARG		L	46.497	57.862	5.698	1.00 58.85	8
	MOTA	5019	N	GLN I	D 12	2	45.507	59.211	4.186	1.00 59.05	7
	ATOM	5020	CA	GLN	D 12	2	46.131	58.596	3.024	1.00 57.95	6
30	MOTA	5021	CB	GLN :			45.345	58.958	1.780	1.00 57.48	6
	MOTA	5022	CG	GLN			44.961	57.767	0.955	1.00 61.67	6 6
	MOTA	5023	CD	GLN			43.773	57.069	1.525	1.00 61.71 1.00 64.71	8
	MOTA	5024		GLN			42.729	57.685	1.698 1.831	1.00 59.81	7
0.5	MOTA	5025		GLN			43.912 47.589	55.784 58.926	2.769	1.00 57.99	6
35	MOTA	5026	C	GLN			48.280	58.169	2.097	1.00 58.62	8
	MOTA	5027	O ,	GLN THR			48.070	60.046	3.291	1.00 57.97	7
	MOTA	5028 5029	N CA	THR			49.452	60.433	3.042	1.00 58.22	6
	ATOM ATOM	5030	СВ	THR			49.520	61.855	2.464	1.00 56.90	6
40	MOTA	5031	OG1				48.907	62.774	3.377	1.00 53.15	8
40	MOTA	5032	CG2				48.808	61.923	1.110	1.00 56.04	6
	ATOM	5033	C	THR			50.361	60.394	4.255	1.00 60.59	6
	MOTA	5034	0	THR	D 1	3	51.589	60.416	4.120	1.00 61.33	8
	MOTA	5035		SER	D · 1	4	49.762	60.335	5.440	1.00 61.87	7
45	ATOM	5036	CA	SER	D 1	4	50.542	60.332	6.669	1.00 61.93	6
	MOTA	5037	СВ	SER			49.634	60.613	7.863	1.00 61.53	6
	MOTA	5038		SER			50.417	60.962	8.988	1.00 62.76	8
	MOTA	5039		SER			51.323	59.035	6.903	1,00 61.38 1.00 62.07	6 8
	MOTA	5040		SER		4	50.922	57.950	6.467	1.00 59.21	7
50	MOTA	5041		ARG		5	52.444	59.175	7.596 7.911	1.00 58.97	6
	ATOM	5042		ARG		5	53.317	58.061 58.087	7.011	1.00 59.72	6
	MOTA	5043		ARG		.5 .5	54.553 54.219	57.978	5.528	1.00 62.38	6
	MOTA	5044		ARG ARG		.5	55.455	57.608	4.738	1.00 63.96	6
55	MOTA	5045 5046		ARG		.5	56.013	56.364	5.254		7
55	MOTA ATOM	5047		ARG		.5	57.207	55.873	4.929	1.00 66.36	б
	ATOM	5048		1 ARG		.5	57.985		4.080	1.00 65.36	7
	MOTA	5049		2 ARG		.5	57.623	54.721	5.457		7
	ATOM	5050		ARG		.5	53.724		9.376		6
60	ATOM	5051		ARG		.5	54.705		9.715		8
	MOTA	5052	N	PRO	D 1	.6	52.967	57.517	10.265	1.00 55.24	7

						-155				
	MOTA	5053	CD	PRO D	16	51.785	56.700	9.935	1.00 51.06	6
	MOTA	5054		PRO D	16	53.200		11.709	1.00 51.86	6
	ATOM	5055		PRO D	16	52.104	56.602	12.236	1.00 49.85	6
	ATOM	5056		PRO D	16	51.031	56.720	11.226	1.00 51.02	6
5	MOTA	5057		PRO D	16	54.580		12.130	1.00 49.97	6
Ŭ	MOTA	5058		PRO D	16	55.034		13.220	1.00 48.83	8
	ATOM	5059		ASP D	17	55.247		11.270	1.00 50.05	7
	ATOM	5060	CA	ASP D	17	56.56		11.612	1.00 53.82	6
	MOTA	5061	CB	ASP D	17	56.79		10.981	1.00 57.43	6
10	ATOM	5062	CG	ASP D	17	55.97		11.666	1.00 63.55	6
	ATOM	5063	OD1	ASP D	17	55.72		12.892	1.00 63.43	8 8
	MOTA	5064	OD2	ASP D	17	55.59		10.985	1.00 66.47	6
	MOTA	5065	С	ASP D	17	57.71		11.218	1.00 52.72 1.00 54.00	8
	MOTA	5066	Ο.	ASP D	17	58.87		11.440		7
15	MOTA	5067	N	VAL D	· 18	57.38		10.653	1.00 50.54 1.00 51.72	6
	MOTA	5068	CA	VAL D	18	58.41		10.209	1.00 52.70	6
	MOTA	5069	CB	VAL D	18	58.35		8.680	1.00 52.70	6
	MOTA	5070		VAL D	18	59.48		8.209 7.998	1.00 53.16	6
	MOTA	5071			18	58.42			1.00 51.90	6
20	MOTA	5072	С	AMP D	18	58.40		10.865 10.716	1.00 50.79	8
	MOTA	5073	0	VAL D	18	57.46		11.586	1.00 52.81	7
	MOTA	5074	N	ILE D	19	59.47		12.280	1.00 54.09	6
	MOTA	5075	CA	ILE D	19	59.64		13.116	1.00 53.08	6
	MOTA	5076	CB	ILE D	19	60.96 62.16		12.194	1.00 53.31	6
25	MOTA	5077		ILE D	19	61.07		14.027	1.00 52.13	6
	MOTA	5078		ILE D	19 19	62.15		15.086	1.00 49.47	6
	MOTA	5079		ILE D	19	59.67	•	11.255	1.00 56.58	6
	MOTA	5080	C	ILE D	19	60.43		10.274	1.00 57.79	8
00	MOTA	5081	0	ILE D	20	58.83		11.464	1.00 56.89	7
30	MOTA	5082	N	PRO D	20	57.93		12.603	1.00 56.43	6
-	MOTA	5083 5084	CD	PRO D	20	58.72		10.587	1.00 58.17	6
	MOTA	5084	CB	PRO D	20	57.50		11.148	1.00 57.33	6
	MOTA	5086	CG	PRO D		56.83		12.009	1.00 56.81	6
35	ATOM ATOM	5087		PRO D		59.9		10.585	1.00 60.38	6
33	ATOM	5088		PRO D	_	59.9		10.802	1.00 57.93	8
	MOTA	5089		THR D		61.1		10.329	1.00 64.41	7
	MOTA	5090		THR D		62.3	92 66.106		1.00 68.99	6
	ATOM	5091		THR D		63.5	46 65.121		1.00 68.83	6
40	ATOM	5092				63.8	99 65.152		1.00 69.74	8
-10	ATOM	5093		2 THR I	21	64.7	60 65.457			6
	MOTA	5094		THR I	21	62.6			1.00 73.81	6
	MOTA	5095		THR I	21	62. <u>4</u>				8
,	ATOM	5096		GLN I		63.1				7 6
45	MOTA	5097	CA	GLN I		63.4				6
	MOTA	5098	CB			62.7				-6
	MOTA	5099	) CG			61.2				6
	MOTA	5100	) CD			60.6				8
	MOTA	5101		1 GLN I						7
50	MOTA	5102		2 GLN I		59.9		_		6
	MOTA	5103		GLN I		65.0				8
	MOTA	5104		GLN I		65.5				7
	MOTA			ARG I		65.6				6
	MOTA					67.1				6
55	MOTA					67.6 67.4				6
	MOTA					66.2		_		6
	ATOM					65.9				7
	ATOM					66.9				6
60	MOTA			ARG						
60				12 ARG						
	ATOM	1 211	- MI	ייי אוויים		551.				

WO 01/58951

								-156				
	MOTA	5114	С	ARG I	D	23		67.768	68.079	8.399	1.00 87.43	6
	ATOM	5115	_	ARG		23		67.201	67.105	8.907	1.00 88.35	8
	ATOM	5116		ASP :		24		68.912	68.570	8.875	1.00 87.68	7
	MOTA	5117	CA	ASP :	D	24		69.538	67.975	10.055	1.00 86.96	6
5	MOTA	5118	CB	ASP :	D	24		71.041	68.283	10.123	1.00 91.11	6
	MOTA	5119	CG	ASP	D	24		71.627	68.719	8.780	1.00 94.40	6
	MOTA	5120	OD1	ASP	D	24		71.599	67.908	7.806	1.00 95.87	8
	MOTA	5121	OD2	ASP	D	24		72.121	69.881	8.712	1.00 95.25	8
	MOTA	5122	C	ASP	D	24		68.864	68.594	11.274	1.00 85.02	6
10	MOTA	5123	0	ASP	D	24		69.279	68.347	12.414	1.00 83.40	8
	MOTA	5124	N	ARG	D	25		67.836	69.409	11.026	1.00 82.95	7
	MOTA	5125	CA	ARG		25		67.112	70.062	12.111	1.00 81.58	6 6
	MOTA	5126	CB	ARG		25		66.218	71.189	11.585	1.00 83.67 1.00 88.52	6
	MOTA	5127	CG	ARG		25		66.951	72.455	11.150	1.00 92.65	6
15	ATOM	5128	CD	ARG		25		65.941	73.597	10.942	1.00 96.29	7
	MOTA	5129	NE	ARG		25		66.579	74.866	10.584	1.00 98.03	6
	MOTA	5130	CZ	ARG		25		65.928	76.024	10.463	1.00 98.05	7
	MOTA	5131		ARG		25		64.608	76.073 77.136	10.673	1.00 98.69	7
~~	MOTA	5132		ARG		25		66.597 66.241	69.091	12.901	1.00 78.66	6
20	MOTA	5133	C	ARG		25		65.480	68.303	12.325	1.00 70.00	8
	MOTA	5134	0	ARG		25		66.353	69.127	14.237	1.00 74.94	7
	MOTA	5135	N	PRO		26 26		67.383	69.831	15.020	1.00 73.76	6
	MOTA	5136	CD	PRO PRO		26		65.562	68.252	15.101	1.00 71.13	6
25	MOTA	5137	CA CB	PRO		26		66.202	68.450	16.483	1.00 71.49	б
25	MOTA MOTA	5138 5139	CG	PRO		26		67.608	68.884	16.165	1.00 72.18	6
	ATOM	5140	C	PRO		26		64.115	68.738	15.095	1.00 67.33	6
	MOTA	5141	Ö	PRO		26		63.834	69.874	14.713	1.00 65.48	8
	ATOM	5142	N	VAL		27		63.198	67.870	15.510	1.00 63.87	7
30	ATOM	5143	CA	VAL		27		61.806	68.258	15.596	1.00 58.65	6
•	ATOM	5144	CB	VAL		27		60.849	67.036	15.494	1.00 57.16	6
	MOTA	5145	CG1	VAL	D	27		59.462	67.401	15.998	1.00 54.11	6
	MOTA	5146	CG2	VAL	D	27		60.755	66.579	14.052	1.00 56.19	6
	MOTA	5147	С	VAL		27		61.705	68.896	16.968	1.00 56.92	6 8
35	MOTA	5148	0	VAL		27		62.164	68.337	17.961	1.00 55.97	7
	MOTA	5149	N	ALA		28		61.136	70.088	17.019	1.00 56.42 1.00 55.56	6
	MOTA	5150	CA	ALA		28	•	60.999	70.767	18.287	1.00 55.33	6
	MOTA	5151	СВ	ALA		28		61.057	72.269	18.095 18.923	1.00 54.28	6
40	MOTA	5152	C	ALA		28		59.688	70.371	18.440	1.00 54.43	8
40	ATOM	5153	0	ALA		28		58.617 59.800	69.603	20.006	1.00 52.62	7
	MOTA	5154	N	VAL		29		58.657	69.127	20.775	1.00 50.60	6
	ATOM	5155	CA	VAL		29		58.715	67.599	21.016		6
	MOTA	5156	CB	VAL VAL		29 29		57.543	67.162	21.871	1.00 46.20	6
45	MOTA	5157 5158	_	VAL		29		58.718	66.868	19.692	1.00 47.60	6
40	MOTA MOTA	5159	C	VAL		29		58.652	69.805	22.131	1.00 50.77	6
	ATOM	5160	0	VAL		29		59.657	69.806	22.852	1.00 51.59	8
	ATOM	5161	N	SER		30		57.517	70.395	22.471	1.00 50.31	7
	ATOM	5162	CA	SER		30		57.373	71.049	23.754	1.00 52.56	6
50	ATOM	5163	СВ	SER		30		56.794	72.449	23.575	1.00 53.44	6
•	ATOM	5164		SER		30		55.514	72.393	22.966	1.00 56.80	8
	ATOM	5165		SER	D	30		56.442	70.188	24.598	1.00 53.29	6
	MOTA	5166		SER	D	30		·55.397	69.746	24.126		8
	ATOM	,5167	N	VAL	D	31		56.845	69.947			7
55	MOTA	5168	CA	VAL		31		56.089	69.130	26.780		6
	MOTA	5169		VAL		31		56.911	67.898	27.241		6
	MOTA	5170		1 VAI		31		56.015	66.914	27.986		6 6
	MOTA	5171		2 VAI		31		57.573	67.234	26.043		6
~~	MOTA	5172		VAI		31		55.753	69.947	28.015 28.570		8
60	ATOM	5173		VAI		31		56.607 54.508	70.632 69.850			7
	MOTA	5174	N	SEF	<b>.</b> D	32		74.700	05.050	. 20,400		•

						-157				
	ATOM	5175	CA	SER D	32	54.062	70.594	29.628	1.00 59.47	6
	ATOM	5176		SER D		53,467	71.934	29.175	1.00 60.04	6
	ATOM	5177	OG	SER D		52.892	72.641	30.256	1.00 62.30	8
	ATOM	5178	С	SER D	32	53.023	69.799	30.433	1.00 58.78	6
5	ATOM	5179	0	SER D	32	51.906	69.572	29.966	1.00 59.54	. 8
	MOTA	5180	N	LEU D	33	53.390	69.379	31.638	1.00 56.81	7
	MOTA	5181	CA	LEU D	33	52.468	68.629	32.472	1.00 56.85	6
	MOTA	5182	CB	LEU D		53.217	67.702	33.426	1.00 54.23	6
	MOTA	5183	CG	LEU D		54.192	66.726	32.775	1.00 55.08	6
10	MOTA	5184		LEU D		54.665	65.709	33.818	1.00 53.15	6
	MOTA	5185		LEU D		53.513	66.034	31.614	1.00 54.80	6 6
	MOTA	5186	С	LEU D		51.623	69.572	33.291	1.00 56.91 1.00 59.29	8
	MOTA	5187	0	LEU D		52.136	70.542	33.829	1.00 55.25	7
4 ==	MOTA	5188	N	LYS D		50.327	69.294 70.089	33.366 34.171	1.00 55.13	6
15 -	ATOM	5189	CA	LYS I		49.422	70.694	33.320	1.00 58.38	6
	ATOM	5190	CB	LYS I		48.311 48.802	71.519	32.146	1.00 55.52	6
	ATOM	5191	CG	LYS I		49.581	72.764	32.581	1.00 69.06	6
	ATOM	5192	CD	LYS I		50.100	73.559	31.364	1.00 72.37	6
20	MOTA	5193 5194	CE NZ	LYS		50.200	74.801	31.747	1.00 72.05	7
20	ATOM	5194	C	LYS I		48.838	69.065	35.118	1.00 53.80	6
	ATOM ATOM	5196	0	LYS I		48.123	68.167	34.685	1.00 55.04	8
	ATOM	5197	N	PHE I		49.144	69.173	36.405	1.00 51.60	7
	ATOM	5198	CA	PHE I		48.616	68.200	37.346	1.00 49.19	6
25	ATOM	5199	· CB	PHE I		49.441	68.199	38.616	1.00 46.49	6
	ATOM	5200	CG	PHE I		50.838	67.733	38.393	1.00 48.31	6
	ATOM	5201		PHE I		51.823	68.617	37.964	1.00 46.94	6
	ATOM	5202		PHE I		51.159	66.387	38.530	1.00 49.16	6
	ATOM	5203		PHE I		53.109	68.170	37.668	1.00 48.04	6
30	ATOM	5204	CE2	PHE I	35	52.449	65.925	38.235	1.00 50.28	6
	ATOM	5205	CZ	PHE I	D 35	53.424	66.818	37.802	1.00 48.13	6
	ATOM	5206	С	PHE I		47.136	68.352	37.642	1.00 49.07	6
	ATOM	5207	0	PHE I		46.626	69.449	37.869	1.00 49.57	8
	MOTA	5208	N	ILE I		46.451	67.217	37.600	1.00 47.68	7
35	MOTA	5209	CA	ILE 1		45.030	67.156	37.827	1.00 44.72	6
	ATOM	5210	CB	ILE :		44.352	66.334	36.731	1.00 43.48	6 6
	ATOM	5211	CG2			42.850	66.369	36.914	1.00 41.45 1.00 43.86	6
	ATOM	5212		ILE :		44.752	66.877	35.360 35.152	1.00 45.80	6
40	MOTA	5213		ILE :		44.398	68.324 66.525	39.164	1.00 44.81	6
40	MOTA	5214	C	ILE :		44.719 43.677	66.798	39.743	1.00 46.51	8
	ATOM	5215	0	ILE :		45.612	65.678	39.661	1.00 42.08	7
	MOTA	5216 5217	N CA	ASN		45.363	65.030	40.939	1.00 42.31	6
	MOTA	5217	CB	ASN		44.117	64.140	40.834	1.00 41.66	6
45	MOTA MOTA	5219	CG	ASN		43.392	63.990	42.159	1.00 43.88	6
70	ATOM	5220		ASN		44.015	63.785	43.200	1.00 43.62	8
	ATOM	5221		ASN		42.068	64.085	42.124	1.00 38.41	7
	ATOM	5222	C	ASN		46.539	64.186	41.426	1.00 43.81	6
	ATOM	5223	ō	ASN		47.380	63.752	40.640	1.00 40.93	8
50	ATOM	5224	N	ILE		46.588	63.977	42.740	1.00 43.93	7
•	ATOM	5225	CA	ILE		47.612	63.163	43.372	1.00 44.58	6
	ATOM	5226	СВ	ILE		48.496	64.013	44.246	1.00 42.93	6
	ATOM	5227	CG2	ILE	D 38	49.473	63.140	44.989	1.00 39.88	6
	MOTA	5228	CG1	ILE	D 38	49.220	65.028	43.359		6
55	MOTA	5229		ILE		49.944	66.110	44.084	1.00 44.94	6
	ATOM	5230		ILE		46.795	62.183	44.190	1.00 47.97	6
	MOTA	5231		ILE		46.169	62.565	45.162	1.00 50.60	8
	ATOM	5232		LEU		46.802	60.916	43.777	1.00 50.68 1.00 51.24	7 6
	MOTA	5233		LEU		45.979	59.874	44.388	1.00 51.24	6
60	ATOM	5234		LEU		45.489	58.944	43.287 42.141	1.00 51.95	6
	MOTA	5235	CG	LEU	D 39	44.834	59.723	46.141	7.00 24.04	U

WO 01/58951

	WO 01/30	9931							PC1/EF01/014	131
						-158				
					20		58.777	41.068	1.00 53.53	6
	MOTA	5236		LEU D	39		60.542	42.696	1.00 53.70	6
	MOTA	5237		LEU D	39	43.666		45.529	1.00 53.82	6
	MOTA	5238		LEU D	39	46.520	59.041	46.479	1.00 54.77	8
	ATOM	5239	_	LEU D	39	45.793	58.750		1.00 54.21	7
5	MOTA	5240		GLU D	40	47.771	58.620	45.437	1.00 56.24	6
	MOTA	5241	CA	GLU D	40	48.349	57.825	46.507	1.00 58.24	6
	MOTA	5242	CB	GLU D	40	48.278	56.339	46.204		
	ATOM	5243	CG	GLU D	40	46.873	55.801	46.103	1.00 65.00	6
	ATOM	5244	CD	GLU D	40	46.844	54.291	45,938	1.00 68.23	6 -
10	ATOM	5245	OE1	GLU D	40	47.443	53.791	44.955	1.00 70.63	8
	ATOM	5246		GLU D	40	46.226	53.611	46.789	1.00 68.96	8
	ATOM	5247	-	GLU D	40	49.785	58.198	46.702	1.00 56.38	6
	ATOM	5248	_	GLU D	40	50.541	58.355	45.746	1.00 59.25	8
	ATOM	5249		VAL D	41	50.162	58.343	47.955	1.00 55.49	7
15	ATOM	5250		VAL D	41	51.517	58.695	48.273	1.00 54.71	6
13		5251		VAL D	41	51.590	60.145	48.811	1.00 55.08	6
	MOTA	5252		VAL D	41	52.954	60.431	49.361	1.00 55.65	6
	MOTA	5253		VAL D	41	51.273	61.125	47.696	1.00 55.07	6
	ATOM		C	VAL D	41	52.003	57.713	49.309	1.00 54.17	6
00	ATOM	5254		VAL D	41	51.232	57.239	50.136	1.00 53.51	8
20	MOTA	5255	Ο .	ASN D	42	53.280	57.381	49.233	1.00 54.90	7
	ATOM	5256	N		42	53.880	56.473	50.182	1.00 56.47	6
	MOTA	5257	CA	ASN D	42	53.944	55.056	49.612	1.00 55.97	6
	MOTA	5258	CB	ASN D		54.306	54.025	50.661	1.00 56.38	6
	MOTA	5259	CG	ASN D	42	55.272	54.191	51.408	1.00 55.15	8
25	MOTA	5260		ASN D	42	53.536	52.947	50.717	1.00 56.12	7
	MOTA	5261		ASN D	42		57.022	50.420	1.00 58.56	6
	MOTA	5262	С	ASN D	42	55.278	56.912	49.567	1.00 58.83	8
	MOTA	5263	0	ASN D	42	56.154		51.579	1.00 59.69	7
	ATOM	5264	N	GLU D	43	55.474	57.639	51.905	1.00 60.97	6
30	ATOM	5265	CA	GLU D	43	56.771	58.208	53.065	1.00 63.50	6
	ATOM	5266	CB	GLU D	43	56.640	59.192		1.00 67.19	6
	ATOM	5267	CG	GLU D	43	57.921	59.959	53.341	1.00 68.84	6
	MOTA	5268	CD	GLU D		57.725	61.121	54.303		8
	MOTA	5269	OE1			58.743	61.734	54.682	1.00 70.83	8
35	MOTA	5270	OE2	GLU D		56.568	61.427	54.670	1.00 67.80 1.00 59.80	6
	ATOM	5271	С	GLU D	43	57.792	57.134	52.246		8
	MOTA	5272	0	GLU D	43	58.993	57.356	52.138	1.00 59.85	7
	ATOM	5273	N	ILE D	44	57.301	55.969	52.653	1.00 59.27	
	ATOM	5274	CA	ILE D	44	58.164	54.858	53.006	1.00 59.05	6
40	ATOM	5275	CB	ILE D	44	57.373	53.723	53.681	1.00 59.62	6
	ATOM	5276	CG2	ILE D	44	58.300	52.527	53.945	1.00 59.50	6
	ATOM	5277		ILE D	44	56.752	54.217	<b>54</b> .982	1.00 58.87	6
	ATOM	5278		ILE D		57.768	54.484	56.073	1.00 60.45	6
	MOTA	5279		ILE D		58.801	54.286	51.751	1.00 59.04	6
45	ATOM	5280		ILE I	44	60.001	54.029	51.723	1.00 60.06	8
.0	ATOM	5281		THR I		57.986	54.080	50.719	1.00 57.12	7
	ATOM	5282		THR I		58.461	53.513	49.464	1.00 54.05	6
	ATOM	5283		THR I		57.410	52.576	48.857	1.00 52.43	6
	ATOM	5284		L THR I		56.204	53.304	48.628	1.00 49.39	8
50	ATOM	5285		THR I		57.128		49.788		6
50	ATOM	5286		THR I		58.833	54.551	48.417	1.00 53.32	6
		5287		THR I		59.427		47.397	1.00 56.15	. 8
	MOTA			ASN I		58.493				7
	MOTA	5288 5289		ASN I		58.796				6
55	ATOM			ASN I		60.305			1.00 51.66	6
55		5290				60.874			1.00 52.73	6
	MOTA			ASN I		62.057			1.00 52.55	8
	ATOM			ASN 2		60.041				7
	ATOM					58.156				6
00	ATOM			ASN		58.820			_	8
60				ASN		56.858				7
	MOTA	529	6 N	GLU	ע 4/	50.050	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			

	WO 01/5	8951							PCT/EPU1/014	157
						-159				
			_		4.5		56.091	45.155	1.00 48.91	6
	MOTA	5297		GLU D	47 .	56.118	54.627	45.105	1.00 46.66	6
	MOTA	5298		GLU D	47	55.717	53.678	45.006	1.00 47.02	6
	MOTA	5299		GLU D	47	56.888	52.227	45.018	1.00 49.64	6
_	ATOM	5300		GLU D	47	56.458	51.956	44.644	1.00 48.30	8
5	MOTA	5301		GLU D	47	55,302	51.357	45.391	1.00 51.88	8
	MOTA	5302		GLU D	47	57.276		45.391	1.00 50.12	6
	ATOM	5303	_	GLU D	47	54.888	56.992	46.125	1.00 50.30	8
	MOTA	5304		GLU D	47	54.222	57.202	43.936	1.00 50.20	7
	MOTA	5305		VAL D	48	54.591	57.531	43.793	1.00 52.05	6
10	MOTA	5306		VAL D	48	53.455	58.423	43.793	1.00 53.36	6
	MOTA	5307	CB	VAL D	48	53.925	59.861	43.352	1.00 56.39	6
	MOTA	5308		VAL D	48	52.727	60.778	44.620	1.00 54.18	6
	MOTA	5309		VAL D	48	54.801	60.352		1.00 51.50	6
	MOTA	5310	С	VAL D	48	52.522	57.995	42.673 41.617	1.00 53.49	8
15	MOTA	5311	0	VAL D	48	52.962	57.552	42.910	1.00 49.46	7
	MOTA	5312	N	ASP D		51.231	58.137	41.920	1.00 49.81	6
	MOTA	5313	CA	ASP D		50.241	57.777 56.813	42,535	1.00 52.06	6
	MOTA	5314	CB	ASP D		49.241	56.086	41.508	1.00 53.16	6
	ATOM	5315	CG	ASP D		48.447	56.719	40.499	1.00 53.36	8
20	MOTA	5316		ASP D		48.086	54.887	41.717	1.00 57.15	8
	MOTA	5317		ASP D		48.176	59.105	41.580	1.00 49.01	6
	MOTA	5318	С	ASP D		49.583	59.105	42.373	1.00 48.57	8
	MOTA	5319	0	ASP D		48.818	59.624	40.394	1.00 48.09	7
	MOTA	5320	N	VAL D		49.882	60.928	39.986	1.00 47.49	6
25	MOTA	5321	CA	VAL D		49.380		39.980	1.00 49.68	6
	MOTA	5322	CB	VAL D		50.561	61.946 61.732	38.761	1.00 49.68	6
	MOTA	5323		VAL I		51.428		40.017	1.00 54.48	6.
	MOTA	5324		VAL I		50.048	63.356 60.966	38.630	1.00 44.84	6
	ATOM	5325	C	VAL I		48.671	60.107	37.791	1.00 46.99	8
30	ATOM	5326	0.	VAL I		48.885	61.971	38.443	1.00 41.91	7
	ATOM	5327	N	VAL I		47.816 47.067	62.186	37.204	1.00 40.48	6
	ATOM	5328	CA	VAL I		45.560	62.225	37.460	1.00 37.45	6
	ATOM	5329	CB	VAL I		44.837	62.697	36.213	1.00 39.17	6
0.5	ATOM	5330		VAL I		45.070	60.860	37.859	1.00 36.64	6
35	ATOM	5331		VAL I		47.479	63.538	36.628	1.00 42.16	6
	ATOM	5332	C	VAL I		47.560	64.508	37.359	1.00 46.47	8
	ATOM	5333	0	VAL I		47.726	63.617	35.328	1.00 40.72	7
	MOTA	5334	N	PHE I		48.144	64.877	34.738	1.00 42.11	6
40	ATOM	5335	CA	PHE I		49.635	65.072	34.984	1.00 41.64	6
40	ATOM	5336	CB	PHE I		50.491	64.007	34.362	1.00 42.87	6
	MOTA	5337	CG CD1			50.887	64.099	33.038		6
	MOTA	5338 5339		PHE	_	50.868	62.891	35.088	1.00 42.70	6
	MOTA	5340		PHE		51.642		32.447	1.00 42.06	6
45	ATOM ATOM	5340		PHE		51.624		34.506	1.00 42.93	6
40	ATOM	5342		PHE		52.010		33.185	1.00 41.42	6
	ATOM	5343		PHE		47.870		33.241	1.00 44.00	6
	ATOM	5344		PHE		47.606		32.610	1.00 46.55	8
	MOTA	5345		TRP		47.934		32.673	1.00 43.89	7
50	MOTA	5346		TRP		47.726		31.253	1.00 44.08	6
50	ATOM	5347		TRP		46.919		30.948	1.00 45.09	6
	MOTA	5348		TRP		45.537		31.396	1.00 46.86	6
	MOTA	5349		2 TRP		44.596		31.383	1.00 49.97	6
	MOTA	5350				43.372		31.855	1.00 50.77	6
55	ATOM	5351		3 TRP		44.666		31.017		6
55	ATOM	5352		1 TRP		44.877				- 6
	ATOM	5353		1 TRP		43.571		32.141		. 7
	ATOM	5354		2 TRP					1.00 52.23	6
	ATOM	535		3 TRP						6
60	ATOM	535		2 TRP			70.126			6
	ATOM	535		TRP				30.640	1.00 46.17	6
			-							

WO 01/58951 PCT/EP01/01457
-160

							-160					_
	ATOM	5358	0	TRP D	5	3	49.803	67.384	30.960	1.00 4		8
	ATOM	5359		GLN D	5	4	49.444	65.532	29.760	1.00 49		7
	MOTA	5360	CA	GLN D	5	4	50.741	65.592	29.112	1.00 4		6
	ATOM	5361		GLN D	5	54	51,248	64.184	28.809	1.00 4		6
5	MOTA	5362	CG	GLN D		4	52.677	64.135	28.317	1.00 5		6
J	ATOM	5363	CD	GLN D		54	53.339	62.792	28.583	1.00 5	2.08	6
	ATOM	5364				54	53,409	62.336	29.721	1.00 5		8
	ATOM	5365		GLN D		54	53.832	62.158	27.532	1.00 5		7
		5366	C	GLN D		54	50.560	66.408	27.849	1.00 4		6
10	ATOM ATOM	5367	0	GLN D		54	50.504	65.892	26.735	1.00 4	8.80	8
10		5368	N	GLN I		55	50.441	67.708	28.058	1.00 5	1.39	7
	MOTA		CA	GLN I		55	50.256	68.665	26.985	1.00 5	3.26	6
	ATOM	5369 5370	CB	GLN I		55	49.964	70.022	27.609	1.00 5	6.68	б
	MOTA	5370	CG	GLN I		55	49.913	71.176	26.652	1.00 6	6.24	6
1 =	ATOM	5371	CD	GLN I		55	49.355	72.406	27.326	1.00 7	0.72	6
15	MOTA			GLN I		55	49.611	72.637	28.525	1.00 7		8
	MOTA	5373	OE1	GLN I		55	48.584	73.210	26.573	1.00 7		7
	MOTA	5374	NE2	GLN I		55	51.494	68.697	26.092	1.00 5		6
	ATOM	5375	C	GLN I		55	52,533	69.249	26.457	1.00 5		8
00	MOTA	5376	0	THR I		56	51.373	68.091	24.920	1.00 4		7
20	MOTA	5377	N			56	52.485	68.005	23.988	1.00 4		6
	MOTA	5378	CA	THR I		56	52.769	66.534	23.617	1.00 4		6
	ATOM	5379	CB	THR I		56	52.793	65.733	24.801	1,00 5		8
	MOTA	5380	OG1			56	54.101	66.408	22.925	1.00 4		6
0=	MOTA	5381	CG2			56	52.198	68.771	22.709	1.00 4		6
25	MOTA	5382	C	THR		56	51.051	68.862	22.275	1,00 5		8
	ATOM	5383	0	THR I		57	53.243	69.320	22.101	1.00		7
	ATOM	5384	N	THR		57	53.080	70.069	20.860	1.00		6
	ATOM	5385	CA	THR		57	52.766	71.563	21.126	1.00		6
00	MOTA	5386	CB	THR		57	51.521	71.679	21.834	1.00		8
30	ATOM	5387	OG1			57	52.642	72.317	19.826	1.00		6
	MOTA	5388		THR			54.322	69.988	19.995	1.00		6
	ATOM	5389	C	THR		57	55.446	69.954	20.496	1.00	48.40	8
	ATOM	5390	0	THR		57	54.113	69.928	18.686	1.00		7
~-	ATOM	5391	N	TRP		58	55.221	69.883	17.749	1.00		6
35	ATOM	5392	CA	TRP		58	55.890	68.501	17.750	1.00		6
	MOTA	5393	CB	TRP		58	55.055	67.379	17.192	1.00		6
	MOTA	5394	CG	TRP		58	54.099	66.585	17.904	1.00		6
	MOTA	5395	CD2			58	53.517	65.702	16.976		45.14	6
	MOTA	5396	CE			58	53.675	66.537	19.240		44.92	6
40	MOTA	5397	CE			58	55.018	66.952	15.902		44.73	6
	ATOM	5398		1 TRP		58	54.097	65.945	15.761		46.01	7
	ATOM	5399		1 TRP	ת	58	52.533	64.783	17.336		46.24	6.
	ATOM	5400		2 TRP		58	52.696	65.618	19.596		45.62	6
4	MOTA	5401		3 TRP		58	52.030	64.755	18.646		45.70	6
45	MOTA	5402		2 TRP		58	54.679	70.236	16.386		47.55	6
	MOTA	5403		TRP		58	53.494		16.237		46.55	8
	MOTA	5404		TRP		58			15.381		51.25	7
	MOTA	5405		SER		59	55.537				54.98	6
	MOTA	5406				59	55.097				56.59	6
50	MOTA	5407				59 50	55.688				61.93	8
	MOTA	5408				59	54.969				55.53	6
	MOTA	5409		SER		59	55.457				54.93	8
	MOTA	5410		SER		59	56.587				57.49	7
	ATOM	5411		ASP		60	54.479				59.17	6
55	MOTA					60	54.660				61.53	6
	ATOM	5413				60	53.898				63.57	6
	MOTA					60	54.141	_			64.52	8
	MOTA			1 ASP		60	54.465				64.89	8
	MOTA			2 ASP		60	53.988				60.52	6
60				ASP		60	54.067				59.95	8
	ATOM	5418	в о	ASP	ם	60	52.847	69.016	, ,,,,,,	, 2.00		

	WO 01/5	58951							PCT/EP01/01	457
						-161				
	ттом	5419	N	ARG D	61	54.937	69.609	8.995	1.00 62.50	7
	ATOM ATOM	5420		ARG D	61	54.503	70.334	7.800	1.00 64.61	6 ·
	ATOM	5421		ARG D	61	55.672	71.137	7.205	1.00 67.57	6
	ATOM	5422		ARG D	61	56.000	72.468	7.909	1.00 73.40	6
5	ATOM	5423	_	ARG D	61	56.968	73.283	7.037	1.00 81.08	6
9	ATOM	5424		ARG D	61	57.268	74.635	7.537	1.00 86.56	7
	ATOM	5425	CZ	ARG D	61	58.057	75.522	6.910	1.00 87.41	6
	ATOM	5426		ARG D	61	58.642	75.210	5.749	1.00 87.01	7
	ATOM	5427		ARG D	61	58.246	76.731	7.433	1.00 87.16	7
10	ATOM	5428	С	ARG D	61	53.867	69.476	6.703	1.00 64.15	6
. •	ATOM	5429	Ō	ARG D	61	53.145	69.998	5.844	1.00 63.51	8
	ATOM	5430	N	THR D	62	54.121	68.170	6.722	1.00 62.13	7
	ATOM	5431	CA	THR D	62	53.542	67.303	5.704	1.00 61.28	6
	ATOM	5432	CB	THR D	62	54.171	65.886	5.716	1.00 62.74	6
15	MOTA	5433	OG1	THR D	62	53.809	65.201	6.924	1.00 65.20	8
	ATOM	5434	CG2	THR D	62	55.692	65.974	5.624	1.00 63.05	6
	ATOM	5435	С	THR D	62	52.030	67.184	5.911	1.00 60.41	6
	ATOM	5436	0	THR D	62	51.313	66.619	5.073	1.00 60.16	8
	ATOM	5437	N	LEU D	63	51.551	67.731	7.025	1.00 59.01	7
20	ATOM	5438	CA	LEU D		50.124	67.705	7.356	1.00 57.25	6 6
	MOTA	5439	CB	LEU D	63	49.932	67.483	8.860	1.00 55.13 1.00 54.37	6
	MOTA	5440	CG	LEU D		50.567	66.242	9.489	1.00 54.37	6
	MOTA	5441		LEU D		50.396	66.277	10.997	1.00 55.32	6
	ATOM	5442	CD2	LEU D		49.917	65.002	8.903	1.00 56.83	6
25	MOTA	5443	С	LEU D		49.446	69.017	6.973	1.00 55.62	8
	ATOM	5444	0	LEU I		48.228	69.091	6.904	1.00 56.52	7
	ATOM	5445	N	ALA I		50.241	70.052	6.730 6.388	1.00 56.94	6
	MOTA	5446	CA	ALA I		49.702	71.362	6.196	1.00 56.75	6
	MOTA	5447	CB	ALA I		50.843	72.351 71.336	5.147	1.00 57.08	6
30	ATOM	5448	С	ALA I		48.825	70.571	4.222	1.00 59.16	8
	MOTA	5449	0	ALA I		49.091	70.371	5.138	1.00 56.39	7
	MOTA	5450	N	TRP I		47.785	72.174	4.008	1.00 57.81	6
	MOTA	5451	CA	TRP I		46.853 45.718	72.200	4.183	1.00 52.06	6
	ATOM	5452	CB	TRP I		44.662	71.708	5.139	1.00 49.69	6
35	ATOM	5453	CG	TRP I		44.574	71.383	6.532	1.00 48.62	6
	ATOM	5454		TRP I		43.386	71.974	7.027	1.00 50.58	6
	MOTA	5455	CE			45.379	70.649	7.409	1.00 45.78	6
	ATOM	5456	CE	1 TRP		43.563	72.466	4.855	1.00 51.37	6
40	ATOM	5457		1 TRP 1		42.787	72.631	5.985	1.00 51.62	7
40	ATOM	5458			•	42.987	71.849	8.358	1.00 48.81	6
	MOTA	5459		2 TRP 3		44.983	70.525	8.731	1.00 45.33	6
	ATOM	5460		2 TRP		43.797	71.122	9.193	1.00 48.88	6
	MOTA	5461 5462		TRP		46.281		3.873	1.00 60.73	6
45	MOTA	5463		TRP		46.309		4.839	1.00 61.78	8
40	MOTA MOTA	5464		ASN		45.757		2.692	1.00 63.62	7
	MOTA	5465				45.198		2.474	1.00 66.29	6
	ATOM	5466				44.996		0.975	1.00 67.13	6
	ATOM	5467				44.462		0.700		6
50	ATOM	5468		1 ASN		44.317		-0.465		8
30	ATOM	5469		2 ASN		44.167	77.866	1.780		7
	ATOM	5470		ASN		43.886	75.676	3.221		6
	ATOM	5471		ASN		42.823		2.820		8
	ATOM	5472		SER		43.982	76.466	4.289		7
55	ATOM	5473				42.852		5.156		6
50	ATOM					43.363		6.586		6
	ATOM					42.519		7.324		8
	ATOM			SER			L 78.025	4.763		6
	ATOM			SER				5.530		8
60				SER				3.589		7 6
	ATOM		9 C2	A SER	D 68	41.538	3 79.805	3.157	7 1.00 79.08	U

	W O 01/3	6751											rc.	LEFUL	01437
							-162	,							
		- 400			٠,				80.	243	1	761	1 00	78.86	6
	MOTA	5480	CB	SER D			41.9		79.			776		79.93	8
	MOTA	5481	OG	SER D			41.6		79.			157	1 00	80.32	6
	MOTA	5482	C	SER D			40.0		80.			552		81.34	8
_	MOTA	5483	0	SER D			39.3					711		80.85	7.
5	ATOM	5484	N	HIS D			39.4		78.					81.81	
	MOTA	5485	CA	HIS D			38.0		78.			663		84.77	
	MOTA	5486	CB	HIS D			37.5		78.			239		88.72	
	ATOM	5487	CG	HIS I			37.8		79.			729			
	ATOM	5488		HIS D			38.7		80.			166		89.11	
10	ATOM	5489		HIS I			37.2		81.			227		88.96	
	MOTA	5490		HIS I		9	37.7		82.			660		90.17	
	ATOM	5491	NE2	HIS I	) 6	9	38.6		81.			188		89.66	
	MOTA	5492	С	HIS I	) 6	9	37.6	507		066		176		81.57	
	MOTA	5493	Ο.	HIS I	6 (	9	36.6	524		459		713		80.65	
15	ATOM	5494	N	SER I	7	0	38.3	362		606		162		80.66	
. •	MOTA	5495	CA	SER I	7	0	38.1	110	75.	319		770		79.33	
	ATOM	5496	CB	SER I	<b>5</b> 7	0	38.8	813	74.	240		941		79.59	
	ATOM	5497	OG	SER I	5 7	0	40.	110	74.	675	3.	. 550		79.40	
	ATOM	5498	С	SER I		0	38.6	624	75.	348	6.	211		77.66	
20	ATOM	5499	ō	SER I		0	39.	520	76.	135	6.	. 545		76.61	
_0	ATOM	5500	N	PRO I		1	38.	037	74.	514	7	. 088		76.20	
	ATOM	5501	CD	PRO I		1	36.	862	73.	660	6	. 801		76.18	
	ATOM	5502	CA	PRO I		1	38.		74.	425	8	.502		74.80	
	ATOM	5503	CB	PRO 1		1	37.		73.	101	8	. 935		75.09	
25	ATOM	5504	CG	PRO		71	36.			.145	8	.196	1.00	75.33	36
20	ATOM	5505	C	PRO 1		1	39.			465	8	.704	1.00	73.29	5 6
	ATOM	5506	o	PRO		71	40.			. 855	7	. 939	1.00	73.93	2 8
		5507	N	ASP		12	40.			.180		.738	1.00	71.19	5 7
	ATOM	5508	CA	ASP		72	41.			.329		.033	1.00	69.88	8 6
20	MOTA		CB	ASP		72	42.			.680		.721		74.5	
30	ATOM	5509		ASP		72	40.			.647		.691		79.1	
	ATOM	5510	CG OD1	. ASP		72		131		.882		.737		79.0	
	MOTA	5511		ASP		72		692		.190		.635		80.5	
	MOTA	5512		ASP		72		330		.212		.923		67.2	
05	ATOM	5513	C			72 72		540		.973		.975		66.5	
35	MOTA	5514	0	ASP GLN		73		421		.556		.637		63.4	
	ATOM	5515	N			73		756		.462		.539		60.9	
	ATOM	5516	CA	GLN		73 73		653		.909		,981		63.1	
	MOTA	5517	CB	GLN			42.			.723		.533		65.5	
40	ATOM	5518	CG	GLN		73 73		460		.099		.957		67.9	
40	MOTA	5519	CD	GLN				413		.692		.216		70.4	
	MOTA	5520		1 GLN		73				.737				69.2	
	MOTA	5521		2 GLN		73		338		.737		.397		58.9	
	MOTA	5522		GLN		73				.445		.029		59.1	
	MOTA	5523	0	GLN		73		639		.108		.737		56.3	
45	MOTA	5524		VAL		74		.317						52.7	
	MOTA	5525				74		.531		.883		3.698		51.3	
	ATOM	5526		VAL		74		.635		.177		329		48.7	
	ATOM	5527		1 VAL		74		.944		.998		.260		48.3	
	MOTA	5528		2 VAL		74		.087		.951		.973		50.7	
50	MOTA	5529	С	VAL		74		.089		.959		3.760		0 49.3	
	MOTA	5530	0	VAL		74		.240		.108		1.173			
	MOTA	5531		SER		75		.264		.023		1.215		0 48.6	
	MOTA	5532	CA			75		.696		.051		5.206		0 46.9	
	MOTA	5533	CB	SER		75		.555		.729		5.166		0 48.4	
55	ATOM	5534	. OG			75		.444		5.718		7.168		0 48.2	
	MOTA	5535		SER	D	75		.159		1.789		1.487		0 44.7	
	MOTA	5536		SER	D	75		.397		.143		3.781		0 43.7	
	ATOM	5537		VAL	D	76		.424		1.449		4.675		0 44.0	
	MOTA	5538		VAL	D	76		.024		3.281		4.039	_	0 43.4	
60	ATOM	5539	СВ			76		.283		3.687		3.264		0 44.	
_	ATOM	5540		1 VAL	D	76	44	.891	62	2.486	1:	2,604	1.0	0 43.	63 6
				•											

							-163				
	ATOM	5541	CG2	VAL I	ο,	76	43.943	64.746	12.241	1.00 42.10	6
	ATOM	5542		VAL I		76	43.419	62.193	15.034	1.00 43.50	6
	ATOM	5543		VAL I		76	44.004	62.472	16.078	1.00 45.44	8
	ATOM	5544		PRO I	D .	77	43.102	60.929	14.721	1.00 42.76	7
5	ATOM	5545	CD	PRO I	D '	77	42.235	60.402	13.656	1.00 41.52	6
	MOTA	5546	CA	PRO I	D	77	43.472	59.865	15.650	1.00 41.41	6
	ATOM	5547	CB	PRO I	D	77	42.856	58.628	15.009	1.00 42.36	6
	ATOM	5548	CG	PRO 1	D.	77	41.674	59.168	14.296	1.00 40.67	6
	ATOM	5549	С	PRO I	D	77	44.985	59.774	15.749	1.00 40.15	6
10	MOTA	5550	0	PRO 1	D	77	45.687	59.922	14.762	1.00 39.02	8
	MOTA	5551	N	ILE :	D	78	45.474	59.537	16.954	1.00 41.66	7
	ATOM	5552	CA	ILE 1	D	78	46.899	59.421	17.217	1.00 42.23	6
	MOTA	5553	CB	ILE :	D	78	47.113	59.019	18.687	1.00 43.04	6
	MOTA	5554	CG2	ILE :	D	78	48.495	58.518	18.924	1.00 45.01	6
15	ATOM	5555	CG1	ILE :	D	78	46.872	60.236	19.555	1.00 47.88	6
	MOTA	5556	CD1	ILE :	D	78	47.618	61.461	19.057	1.00 48.43	6
	MOTA	5557	С	ILE	D	78	47.591	58.432	16.299	1.00 42.53	6
	MOTA	5558	0	ILE	D	78	48.717	58.643	15.880	1.00 44.25	8
	MOTA	5559	N	SER	D	79	46.891	57.358	15.979	1.00 43.93	7
20	ATOM	5560	CA.	SER		79	47.410	56.302	15.127	1.00 43.22	6
	MOTA	5561	CB	SER		79	46.457	55.110	15.185	1.00 42.69	6
	ATOM	5562	OG	SER		79	45.130	55.523	14.910	1.00 43.59	- 8 - 6
	MOTA	5563	С	SER		79	47.661	56.692	13.668	1.00 42.26	8
	ATOM	5564	0	SER		79	48.319	55.953	12.937	1.00 41.56 1.00 39.86	7
25	MOTA	5565	N	SER		80	47.138	57.835	13.243		6
	MOTA	5566	CA	SER		80	47.326	58.282	11.871	1.00 40.25 1.00 40.77	6
	ATOM	5567	СВ	SER		80	46.026	58.840	11.307	1.00 48.70	8
	ATOM	5568	OG	SER		80	45.025	57.845	11.259 11.742	1.00 41.01	6
00	ATOM	5569	C	SER		80	48.413	59.342 59.842	10.655	1.00 41.01	8
30	ATOM	5570	0	SER		80	48.658	59.671	12.847	1.00 39.67	7
	ATOM	5571	N	LEU		81	49.067 50.112	60.678	12.844	1.00 39.96	6
	MOTA	5572	CA	LEU		81	49.703	61.886	13.684	1.00 40.31	6
	ATOM	5573	CB	LEU		81	48.371	62.571	13.448	1.00 42.96	6
25	ATOM	5574	CG CD1	LEU		81 81	48.019	63.429	14.638	1.00 41.75	6
35	ATOM	5575	_	LEU		81	48.454	63.382	12.191	1.00 44.21	6
	ATOM ATOM	5576 5577	CD2	LEU		81	51.357	60.109	13.472	1.00 38.80	6
		5578	0.	LEU		81	51.303	59.077	14.119	1.00 39.28	. 8
	MOTA MOTA	5579	N.	TRP		82	52.478	60.795	13.276	1.00 37.55	7
40	ATOM	5580	CA	TRP		82	53.726	60.398	13.891	1.00 36.02	6
70	ATOM	5581	CB	TRP		82	54.927	60.981	13.158	1.00 39.06	6
	ATOM	5582	CG	TRP		82	56.206	60.891	13.958	1.00 40.02	6
	ATOM	5583		TRP		82	56.715	61.864	14.887	1.00 39.10	6
	ATOM	5584		TRP		82	57.878	61.318	15.463	1.00 38.66	6
45	ATOM	5585		TRP		82	56.294	63.140	15.292	1.00 38.90	6
	ATOM	5586		TRP		82	57.060	59.840	14.007	1.00 40.23	6
	ATOM	5587		TRP		82	58.065	60.082	14.908	1.00 40.21	7
	ATOM	5588		TRP		82	58.630	61.997	16.422	1.00 36.80	6
	MOTA	5589	CZ3	TRP	D	82	57.038	63.812	16.247	1.00 40.18	б
50	MOTA	5590	CH2	TRP	D	82	58.195	63.238	16.801	1.00 38.54	.6
	ATOM	5591	С	TRP	D	82	53.606	61.068	15.236	1.00 35.47	6
	MOTA	5592	Ō	TRP	D	82	53.085	62.172	15.339	1.00 36.72	8
	MOTA	5593	N	VAL	D	83	54.078	60.408	16.272	1.00 34.62	7
	MOTA	5594	CA	VAL	D	83	53.996	60.989	17.592	1.00 36.17	6
55	MOTA	5595	CB	VAL		83	52.827	60.341	18.381	1.00 35.89	6
	MOTA	5596		VAL		83	52.906	60.676	19.835	1.00 38.30	
	MOTA	5597	CG2	VAL		83	51.507	60.840	17.832	1.00 35.92	
	ATOM	5598	С	VAL		83	55.335	60.810	18.312	1.00 37.27	
	ATOM		0	VAL		83	56.035	59.821	18.113	1.00 36.95 1.00 35.49	
60	MOTA	5600	N	PRO		84	55.727	61.796	19.125	1.00 35.49	
	ATOM	5601	CD	PRO	D	84	55.073	63.095	19.324	1.00 3/.20	O

WO 01/58951

	W O 01/5	0751								I CI/LI 01/01	•••
							-164				
	» mom	5602	CA	PRO	ח	84	56.979	61.740	19.873	1.00 36.59	6
	ATOM	5603	CB.	PRO		84	56,933	63.024	20.694	1.00 37.18	6
	ATOM ATOM	5604	CG	PRO		84	56,196	63.930	19.835	1.00 36.05	6
	ATOM	5605	C	PRO		84	57.034	60.502	20.759	1.00 35.92	6
5		5606	0	PRO		84	56.070	60.197	21.449	1.00 34.78	8
5	MOTA	5607	N	ASP		85	58.161	59.798	20.749	1.00 33.98	7
	MOTA	5608	CA	ASP		85	58.283	58.609	21.565	1.00 34.25	6
	MOTA	5609	CB	ASP		85	59.244	57.622	20.925	1.00 35.35	6
	MOTA	5610	CG	ASP		85	60.600	58.201	20.700	1.00 38.15	6
10	MOTA	5611		ASP		85	60.645	59.379	20.327	1.00 40.37	8
10	MOTA	5612		ASP		85	61.612	57.486	20.870	1.00 36.29	8
•	ATOM	5613	C	ASP		85	58.740	58.962	22.964	1.00 37.26	6
	MOTA	5614	0	ASP		85	59.737	58.449	23.453	1.00 38.45	8
	MOTA			LEU		86	57.981	59.840	23.609	1.00 35.72	7
15	MOTA	5615 5616	N CA	LEU		86	58,290	60.294	24.956	1.00 37.34	6
15	MOTA	5616 5617	CB	LEU		86	57.397	61.471	25.325	1.00 35.58	6
	MOTA	5618	CG	LEU		86	57.576	62.690	24.434	1.00 36.77	6
	MOTA	5619		LEU	,	86	56.652		24.877	1.00 32.58	6
	MOTA			LEU		86	59.026		24.496	1.00 36.92	6
20	ATOM	5620		LEU		86	58.112		25.989	1.00 38.80	6
20	MOTA	5621	С 0	LEU		86	57.250		25.853	1.00 43.05	8
	MOTA	5622	N	ALA		87	58.925		27.033	1.00 38.29	7
	ATOM	5623		ALA		87	58.852		28.103	1.00 38.34	6
	ATOM	5624	CA	ALA		87	59.808		27.827	1.00 37.03	6
05	MOTA	5625	CB	ALA		87	59.202		29.414	1.00 39.60	6
25	ATOM	5626	C			87	60.087		29.436	1.00 43.32	8
	ATOM	5627	0	ALA		88	58.495		30.492	1.00 39.86	7
	MOTA	5628	N	ALA		88	58.804		31.786	1.00 39.70	6
	MOTA	5629	CA	ALA		88	57.572		32.654	1.00 38.81	6
20	ATOM	5630	CB	ALA		88	59.861		32.418	1.00 41.02	6
30	MOTA	5631	C	ALA		88	59.575		32.894	1.00 42.74	8
	MOTA	5632	0	ALA		89	61.095		32.400	1.00 42.88	7
	MOTA	5633	N	TYR		89	62.241		32.931	1.00 44.50	6
	MOTA	5634	CA	TYR		89	63.443		33.031	1.00 46.85	6
0.5	MOTA	5635	CB	TYF		89	63.940		31.709	1.00 50.97	6
35	MOTA	5636	CG			89	64.91		31.663	1.00 55.21	6
	ATOM	5637	CD1	TYF TYF		89	65.384		30.441	1.00 57.34	6
	MOTA	5638		YYF		89	63.45		30.502	1.00 52.68	6
	MOTA	5639				89	63.91		29.288	1.00 55.92	6
40	ATOM	5640	CE2	TYF		89	64.88		29.260	1.00 57.40	6
40	ATOM	5641	CZ	TYF		89	65.34		28.048	1.00 61.62	8
	ATOM	5642	ОН		(D	89	62.04		34.274	1.00 43.55	6
	ATOM	5643	C			89	62.61		34.503	1.00 43.31	8
	MOTA	5644			1 D 5 D	90	61.26		35.171	1.00 40.99	7
4=	ATOM	5645			1 D	90	61.05		36.470	1.00 40.89	6
45	ATOM	5646			1 D	90	61.45		37.605	1.00 38.07	6
	ATOM	5647			1 D		60.71		37.561	1.00 38.20	6
	ATOM	5648		1 ASI			60.60		36.515	1.00 43.00	8
	ATOM	5649					60.22				7
ΕO	MOTA	5650		2 ASI			59.64		36.669		6
50	MOTA	5651			N D		59.17		37.795		8
	MOTA	5652			N D		58.97		35,562		7
	MOTA	5653			A D		57.63		35.630		6
	ATOM	5654			A D		56.98		34.260		6
EE	ATOM	5655			A D		57.82		36.150		6
55	ATOM	5656			A D A D		58.71				8
	MOTA	5657			E D		56.96				7
	MOTA	5658			EC		57.01				6
	ATOM	5659			EI		56.83				6
60	MOTA	5660		2 IL			55.42			_	6
60	MOTA						57.82				6
	ATOM	5662	ال د	1 IL	ـ ن	, 54	57.02	,		-	

WO 01/58951

						-165				
	ATOM	5663	CD1	ILE D	92	57.559	52.447	41.544	1.00 57.95	6
	ATOM	5664	C	ILE D	92	55.921	51.998	37.180	1.00 43.63	6
	ATOM	5665		IFE D	92	55.867	50.816	37.502	1.00 43.77	8
	ATOM	5666	N	SER D	93	55.051	52.546	36.343	1.00 41.02	7
5	ATOM	5667	CA	SER D	93	53.968	51.788	35.733	1.00 39.43	6
. –	ATOM	5668	CB	SER D	93	52.673	51.994	36.498	1.00 40.39	6
	ATOM	5669	OG	SER D	93	52.200	53.324	36.320	1.00 40.98	8 6
	ATOM	5670	С	SER D	93	53.802	52.387	34.366	1.00 39.82 1.00 38.78	8
	ATOM	5671	0	SER D	93	54.349	53.452	34.103	1.00 38.78	7
10	MOTA	5672	N	LYS D	94	53.063	51.727	33.484 32.173	1.00 40.02	6
	MOTA	5673	CA	LYS D	94	52.883	52.322 51.260	31.081	1.00 42.12	6
	MOTA	5674	CB	LYS D	94	52.695	50.113	31.405	1.00 45.31	6
	MOTA	5675	CG	LYS D	94	51.789 51.980	48.999	30.378	1.00 48.12	6
<b>.</b> –	MOTA	5676	CD	LYS D	94 94	51.973	49.545	28.957	1.00 49.66	6
15	ATOM	5677	CE	LYS D	94	52.092	48.466	27.938	1.00 53.06	7
	ATOM	5678	NZ	LYS D	94	51.738	53.319	32.205	1.00 42.30	6
	ATOM	5679	C	LYS D	94	50.899	53.299	33.104	1.00 42.15	8
	MOTA	5680	0	PRO D	95	51.707	54.230	31.234	1.00 41.20	7
20	MOTA	5681	N CD	PRO D	95	52.637		30.108	1.00 37.85	6
20	ATOM	5682 5683	CA	PRO D	95	50.655	55.243	31.178	1.00 40.86	6
	MOTA	5684	CB	PRO D	95	51.064	56.117	29.990	1.00 41.55	6
	ATOM	5685	CG	PRO D	95	52.512	55.834	29.821	1.00 42.69	6
	ATOM	5686	C	PRO D	95	49.263	54.691	30.981	1.00 39.96	6
25	MOTA ATOM	5687	0	PRO D	95	49.030	53.893	30.080	1.00 39.70	8
25	ATOM	5688	N	GLU D	96	48.344	55.113	31.835	1.00 40.14	7
	ATOM	5689	CA	GLU D	96	46.961	54.718	31.689	1.00 38.41	6
	ATOM	5690	СВ	GLU D	96	46.321	54.399	33.041	1.00 40.63	6
	ATOM	5691	CG	GLU D		44.880	53.856	32.923	1.00 48.74	6
30	ATOM	5692	CD	GLU D		44.232	53.503	34.273	1.00 51.27	6
00	ATOM	5693		GLU D		44.983	53.350	35:261	1.00 50.19	8
	ATOM	5694	OE2		_	42.979	53.360	34.345	1.00 50.07	8
	ATOM	5695	С	GLU D	96	46.324	55.963	31.084	1.00 37.34	6
	ATOM	5696	0	GLU D	96	45.998	56.900	31.799	1.00 36.63	8
35	ATOM	5697	N	VAL D	97	46.199	55.988	29.760	1.00 34.71	7
	MOTA	5698	CA	VAL I	97	45.599	57.120	29.079	1.00 32.69	6
•	MOTA	5699	СВ	VAL I	97	45.881	57.066	27.582	1.00 30.58	6
	ATOM	5700		L VAL I		45.289	58.260	26.896	1.00 30.36	6 6
	ATOM	5701	CG2	VAL I		47.361	57.037	27.354	1.00 28.89 1.00 34.47	6
40	MOTA	5702	С	VAL I		44.104	57.067	29.345	1.00 34.47	8
	MOTA	5703	0	VAL I		43.431	56.124	28.962	1.00 35.68	7
	MOTA	5704		LEU I		43.597	58.091	30.019	1.00 35.00	6
	MOTA	5705		LEU I		42.190	58.174	30.401 31.713	1.00 35.92	6
	ATOM	5706		LEU I		42.071	58.943	32.894	1.00 36.85	6
45	ATOM	5707		LEU I		42.941	58.547 59.639	33.914	1.00 35.58	6
	MOTA	5708		1 LEU I		42.906	57.261	33.487	1.00 39.84	6
	MOTA	5709		2 LEU 1		42.456 41.276	58.845	29.386	1.00 38.24	6
	MOTA	5710		LEU I		40.055	58.850	29.549	1.00 37.04	8
	MOTA	5711		LEU 1		41.862		28.338	1.00 37.00	7
50	MOTA	5712		THR	-	41.082			1.00 36.28	6
	MOTA	5713				41.449			1.00 36.19	6
	ATOM	5714	1 CB	THR :		42.863			1.00 38.29	8
	ATOM					41.075			1.00 31.31	6
<b>E</b> E	MOTA			2 THR THR		41.224			1.00 35.89	6
55	MOTA			THR		42.148			1.00 35.45	8
	MOTA				D 100	40.281			1.00 34.88	7
	ATOM				D 100	39.043				6
	ATOM ATOM		•		D 100	40.303			1.00 33.36	6
60	MOTA MOTA				D 100	39.217				. 6
JU	ATOM				D 100	38.223		24.093	1.00 33.73	ε
	ATOM									

	WO 01/58	8951								PCT	/EP01/01	<b>457</b>
				:			-166					
	3 501/	5724	_	PRO D	100		41.666	59.955	23.077	1.00	35.04	6
	MOTA	5724 5725		PRO D			42.188	61.028	23.310	1.00		8
	ATOM ATOM	5726		GLN D			42.256	59.026	22.350	1.00		7
	ATOM	5727		GLN D			43.574	59.280	21.817	1.00		6
5	ATOM	5728		GLN D			44.356	57.980	21.749	1.00		6
J	ATOM	5729		GLN D			44.890	57.613	23.109	1.00	41.80	6
	ATOM	5730		GLN D			45.318	56.175	23.201	1.00	46.38	6
	ATOM	5731		GLN D			46.158	55.714	22.439	1.00	50.42	8
	ATOM	5732		GLN D			44.735	55.447	24.143		49.13	7
10	ATOM	5733	C	GLN D			43.543	59.994	20.486		39.27	6
	ATOM	5734	ō	GLN D			43.965	59.463	19.463		38.19	8
	MOTA	5735	N	LEU D			43.037	61.224	20.540		40.46	7
	ATOM	5736	CA	LEU D			42.910	62.103	19.381		40.51	6
	ATOM	5737	CB	LEU D	102		41.467	62.590	19.231		37.39	6
15	MOTA	5738	CG	LEU D			40.382	61.515	19.121		38.97	6
	MOTA	5739		TEA D			39.030	62.182	18.988		36.48	6
	MOTA	5740	CD2	TEA D			40.657	60.628	17.925		36.34	6
	MOTA	5741	С	LEU D			43.804	63.308	19.554		41.42	6
	MOTA	5742	0	TEA D			43.990	63.794	20.665		43.09	8 7
20	MOTA	5743	N	ALA D			44.375	63.777	18.455		40.44 40.53	6
	MOTA	5744	CA	ALA D			45.221	64.953	18.489		43.43	6
	MOTA	5745	CB	ALA D			46.549	64.673	17.847 17.731		41.82	6
	ATOM	5746	C	ALA D			44.500 43.503	66.050 65.803	17.751		41.33	8
05	MOTA	5747	0	ALA D			44.998	67.271	17.849		42.58	7
25	MOTA	5748	N	ARG D			44.369	68.381	17.165		43,20	6
	ATOM	5749	CA	ARG D			43.995	69.450	18.183		43.57	6
	MOTA	5750	CB CG	ARG I			43.032	70.480	17.678		40.98	6
	MOTA	5751 5752	CD	ARG I			41.674	69.900	17,425		39.96	6
30	ATOM ATOM	5753	NE	ARG I			40.803	70.951	16.909		41.32	7
30	ATOM	5754	CZ	ARG I			39.517	70.802	16.635		39.52	6
	ATOM	5755		ARG I		,	38.927	69.633	16.824		40.96	7
	MOTA	5756		ARG I			38.826	71.832	16.175	1.00	38.44	7
	MOTA	5757	C	ARG I			45.380	68.896	16.162		43.89	6
35	MOTA	5758	0	ARG I			46.508	69.192	16.526		44.97	8
	ATOM	5759	N	VAL I			44.989	68.966	14.894		44.88	7
	ATOM	5760	CA	VAL I			45.910	69.427	13.863		46.87	, 6
	MOTA	5761	CB	VAL I			46.094	68.380	12.751		44.91	6
	MOTA	5762		VAL I			47.165	68.838	11.787		42.60	. 6
40	ATOM	5763		VAL I			46.469	67.050	13.346		43.58	6
	MOTA	5764	С	VAL I			45.467				48.29	6
	ATOM	5765	0		105		44.335	70.845	12.731		47.85 48.47	8 7
	ATOM	5766			D 106		46.375	71.702	13.238		50.73	6
	MOTA	5767	CA		106		46.129	73.018	12.663 13.472		50.75	6
45	MOTA	5768	CB		106		46.855	74.106	13.472		51.23	6
	MOTA	5769		VAL 1			46.392 46.601	75.477 73.903	14.951		48.01	6
	MOTA	5770		VAL	D 106		46.636	73.025	11.216		51.91	6
	MOTA	5771			D 106		47.664	72.420	10.918		52.36	8
50	MOTA	5772 5773			D 107		45.920	73.712	10.329		52.06	7
50	ATOM ATOM	5774			D 107		46.281	73.761	8.915		51.56	6
	ATOM	5775			D 107		45.391	74.756	8.185		52.91	6
	ATOM	5776			D 107		45.259	75.941	8.943		59.44	8
	ATOM	5777			D 107		47.726	74.058	8.591	1.00	50.83	6
55	MOTA	5778			D 107		48.188	73.739	7.511		50.82	8
	MOTA	5779			D 108		48.451	74.657	9.519		53.72	7
	MOTA	5780			D 108		49.853	74.978	9.262		57.12	6
	MOTA	5781		ASP	D 108		50.239		9.965		58.24	6
	MOTA	5782	CG		D 108		50.271				61.04	6
60	ATOM	5783		1 ASP			49.396				63.89	8
	ATOM	5784	OD:	2 ASP	D 108		51.162	76.782	12.095	Τ.0(	60.97	8

	WO 01/58	951							•	PCT	<b>/EP01/0</b> 1	1457
							-167					
	ATOM	5785	С	ASP			50.827	73.870	9.665		58.88	6
	ATOM	5786	0	ASP			52.043	74.071	9.635		61.62	8
	ATOM	5787	N	GLY			50.293	72.711	10.051		58.94	7
_	MOTA	5788	CA	GLY			51.134	71.589	10.437		58.18	6
5	ATOM	5789	C	GLY			51.424	71.483	11.918		57.62	6
	MOTA	5790	0	GLY			52.186	70.612	12.343		56.21	8
	ATOM	5791	N	GLU			50.831	72.370	12.707		58.61	7
	MOTA	5792	CA	GLU			51.042	72.345	14.152		59.21	6
10	MOTA	5793	CB	GLU			50.664	73.700	14.776		62.41	6
10	ATOM	5794	CG	GLU			51.327	74.002	16.134		66.58	6
	MOTA	5795	CD OF	GLU			52.852	74.104	16.041		69.79 70.58	6 8
	ATOM ATOM	5796 5797	OE1 OE2	GLU GLU			53.375 53.527	74.340 73.963	14.921 17.089		70.38	8
	ATOM	5798	C	GLU			50.158	71.232	14.712		56.76	6
15	ATOM	5799	0	GLU			49.001	71.079	14.320		54.86	8
,,	ATOM	5800	N	VAL			50.723	70.451	15.625		55.23	7
	ATOM	5801	CA	VAL			50.013	69.333	16.236		53.43	6
	ATOM	5802	СВ	VAL			50.704	67.976	15.889		53.47	6
	ATOM	5803		VAL			49.934	66.821	16.500		51.83	6
20	ATOM	5804		VAL			50.798	67.803	14.382		52.57	6
	MOTA	5805	C	VAL			49.962	69.470	17.754		53.05	6
	ATOM	5806	0	VAL	D	111	50.972	69.747	18.400		52.81	8
	ATOM	5807	N	LEU	D	112	48.783	69.269	18.323		51.91	7
	MOTA	5808	CA	LEU			48.631	69.354	19.766	1.00	51.71	6
25	ATOM	5809	CB	LEU	D	112	47.776	70.566	20.155	1.00	55.12	6
	MOTA	5810	CG	LEU	D	112	47.832	71.901	19.392	1.00	55.82	6
	MOTA	5811	CD1	LEU			49.269	72.287	19.035	1.00	56.65	6
	ATOM	5812	CD2	LEU			46.985	71.777	18.155		55.54	6
~~	MOTA	5813	С	LEU			47.959	68.089	20.292		51.46	б
30	ATOM	5814	0	LEU			46.833	67.769	19.900		51.33	8
	ATOM	5815	N			113	48.659	67.365	21.162		48.43	7
	ATOM	5816	CA			113	48.128	66.149	21.762		45.71	6
	ATOM	5817	CB	TYR			48.941	64.928	21.318		43.52	6
35	ATOM	5818	CG			113	48.490	63.601	21.918		41.37	6
33	ATOM ATOM	5819 5820	CE1	.TYR TYR			47.142 46.735	63.255 62.028	21.975 22.492		39.60 38.43	6 6
	ATOM	5821		TYR			49.423	62.679	22.492		40.11	6
	ATOM	5822	CE2	TYR			49.028	61.458	22.911		39.17	6
	ATOM	5823	CZ			113	47.682	61.134	22.958		40.31	6
40	ATOM	5824	OH	TYR			47.283	59.921	23.470		40.08	8
	MOTA	5825	C			113	48.218		23.262		45.22	6
	ATOM	5826	Ō	TYR	D	113	49.302	66.442	23.812		44.34	8
	MOTA	5827	N	MET	D	114	47.073	66.352	23.924		47.16	7
	MOTA	5828	CA	MET	D	114	47.044	66.541	25.368	1.00	48.56	6
45	MOTA	5829	CB	MET	D	114	46.457	67.906	25.681	1.00	53.17	6
	MOTA	5830	CG	MET	D	114	46.536	68.281	27.130	1.00	58.47	6
	MOTA	5831	SD	MET	D	114	45.470	69.687	27.429	1.00	64.86	16
	MOTA	5832	CE			114	46.527	70.991	26.840	1.00	63.87	6
	MOTA	5833	С			114	46.214	65.472	26.062		47.72	6
50	MOTA	5834	0			114	45.060	65.705	26.424		47.31	8
	MOTA	5835	N			115	46.790	64.279	26.251		45.85	7
٠	MOTA	5836	CD			115	48.108	63.831	25.761		45.44	6
	MOTA	5837	CA			115	46.080	63.184	26.903		44.65	6
55	MOTA	5838	CB			115	46.818	61.967	26.385		46.29	6
J	MOTA MOTA	5839 5840	CG C			115 115	48.231 46.159	62.454 63.283	26.372 28.416		45.12 44.40	6 6
	ATOM	5840 5841	0			115	40.139	63.787	28.416		44.40	8
	ATOM	5842	Ŋ			116	45.124	62.811	29.102		42.71	7
	ATOM	5843	CA			116	45.142	62.828	30.551		40.50	6
60	ATOM	5844	CB			116	43.752	62.976	31.110		37.94	6
-	ATOM	5845	OG			116	43.829	63.015	32.516		44.37	8

	WO 01/5	8951							PCT	/ <b>EP01</b> /01	1457
						-168					
	MOTA	5846	С	SER I		45.712	61.484	30.957	1.00		6
	MOTA	5847	0	SER I		45.190	60.448	30.569	1.00		8
	ATOM	5848	N	ILE I		46.781	61.493	31.739	1.00		7
_	ATOM	5849	CA	ILE I		47.409	60.252	32.135	1.00		6 6
5	MOTA	5850	CB	ILE I		48.842 49.545	60.179 58.932	31.565 32.041	1.00		6
	MOTA MOTA	5851 5852		IPE I		48.802	60.188	30.045	1.00		6
	ATOM	5853		IPE I		50.137	60.454	29.422	1.00		6
	ATOM	5854	CDI	ILE I		47.506	60.000	33.635	1.00		6
10	ATOM	5855	0	ILE I		47.838	60.894	34.407	1.00		8
. •	ATOM	5856	N	ARG I		47.196	58.773	34.042	1.00		7
	ATOM	5857	CA	ARG I		47.356	58.386	35.429	1.00		6
	ATOM	5858	CB	ARG I	118	46.151	57.623	35.966	1.00		6
	ATOM	5859	CG	ARG I	118	46.420	57.119	37.377	1.00		6
15	MOTA	5860	CD	ARG I		45.196	56.638	38.101	1.00		6
	MOTA	5861	NE	ARG I		45.554	56.131	39.414		36.89	7
	ATOM	5862	CZ	ARG I		44.687	55.838	40.367	1.00		6
	ATOM	5863		ARG I		43.396	56.001	40.163		38.10 35.81	7 7
20	ATOM	5864		ARG I	0 118	45.118	55.381 57.469	41.523 35.376		39.50	6
20	MOTA	5865 5866	C		118	48.581 48.661	56.579	34.541		39.41	8
	ATOM ATOM	5867	O N		D 119	49.541	57.678	36.260		39.25	7
	ATOM	5868	CA		D 119	50.739	56.865	36.222		40.77	6
	ATOM	5869	CB		D 119	51.588	57.357	35.059		39.61	6
25	ATOM	5870	CG		D 119	52.879	56.638	34.807		39.00	6
	ATOM	5871	CD		D 119	53.483	57.037	33.476	1.00	37.41	6
	MOTA	5872	OE1	GLN :	D 119	53.349	58.169	33.043	1.00	42.14	8
	MOTA	5873	NE2	GLN :	D 119	54.154	56.112	32.831		38.80	7
	MOTA	5874	С		D 119	51.491	56.961	37.534		42.32	6
30	MOTA	5875	Ó		D 119	51.421	57.965	38.213		43.53	8
	MOTA	5876	N		D 120	52.197	55.908	37.906		43.85	7
	ATOM	5877	CA		D 120	52.950	55.944	39.149		47.43	6
	MOTA	5878	CB		D 120	52.819	54.632 54.278	39.900 40.235		50.39 58.64	6 6
35	ATOM	5879	CG		D 120	51.389 51.352	53.441	41.493		64.21	6
33	MOTA MOTA	5880 5881	CD NE		D 120	51.332	54.244	42.725		67.25	7
	ATOM	5882	CZ		D 120	52.129	53.942	43.790		65.70	6
	ATOM	5883			D 120	52.911	52.870	43.763		64.48	7
	MOTA	5884			D 120	52.049	54.678	44.895		62.69	7
40	MOTA	5885	С		D 120	54.411	56.231	38.913		46.83	6
	MOTA	5886	0	ARG	D 120	54.969	55.848	37.885	1.00	46.53	8
	MOTA	5887	N	PHE	D 121	55.032	56.912	39.869		45.77	7
	MOTA	5888	CA		D 121	56.443	57.249	39.743		45.26	6
	MOTA	5889	CB		D 121	56.627	58.737	39.416		42.47	6
45	MOTA	5890	CG		D 121	55.893	59.186	38.199		41.19	6
	MOTA	5891			D 121	54.546	59.483	38,266		39.80 39.10	6
	MOTA	5892			D 121	56.544	59.284	36.979 37.141		39.10	6 6
	MOTA	5893			D 121 D 121	53.855 55.862	59.872 59.670	35.858		37.48	6
50	ATOM ATOM	5894 5895	CEZ		D 121	54.512	59.965	35.937		38.89	6
50	ATOM	5896	C		D 121	57.256	56.947	40.980		46.08	6
	MOTA	5897	Ö		D 121	56.729	56.783	42.077		43.10	8
	ATOM	5898	N		D 122	58.560	56.881	40.769		48.75	7
	ATOM	5899	CA		D 122	59.520	56.672	41.837	1.00	51.22	6
55	MOTA	5900	СВ	SER	D 122	60.535	55.604	41.442	1.00	51.58	
	MOTA	5901	OG		D 122	61.510	55.455	42.453		51.33	8
	MOTA	5902	С		D 122	60.224	58.027	42.004		51.78	6
	ATOM	5903	0		D 122	60.968	58.460	41.123		50.44	8
00	ATOM	5904	N		D 123	59.965	58.699	43.120		52.36	7
60	MOTA	5905	CA		D 123	60.564	59.999	43.370		55.03	. 6
	ATOM	5906	С	CYS	D 123	60.584	60.314	44.860	T.00	57.50	6

	WO 01/58	8951									PCT	EP01/01	457
								-169					
	ATOM	5907	Ο.	CYS			6	0.131	59.513	45.676	1.00	58.47	8
	MOTA	5908	CB	CYS				9.784	61.083	42.631		54.89	6
	MOTA	5909	SG	CYS				8.043	61.147	43.136		52.88	16
_	ATOM	5910	N	ASP				1.104	61.487	45.218		58.85	7
5	ATOM	5911	CA	ASP				1.196	61.865	46.619		59.59	6
	ATOM	5912	СВ	ASP				2.205	62.994	46.816		60.38	6
	ATOM	5913	CG	ASP				2.876	62.937	48.182		61.57	6
	ATOM	5914		ASP				2.207	62.519	49.151		60.87	8
10	ATOM	5915		ASP				4.067	63.306	48.289		61.86	8
10	MOTA	5916	C	ASP ASP				9.864 9.310	62.294	47.198		59.72 59.12	6 8
	ATOM ATOM	5917 5918	N O	VAL				9.366	63.329 61.492	46.822 48.131		60.02	7
	ATOM	5919	CA	VAL				8.096	61.758	48.795		61.00	6
	ATOM	5920	CB	VAL				7.274	60.469	48.906		57.98	6
15	ATOM	5921		VAL				6.007	60.721	49.664		56.31	6
	ATOM	5922		VAL				6.973	59.946	47.526		58.88	6
	MOTA	5923	C	VAL				8.305	62.346	50.199		63.48	6
	ATOM	5924	ō	VAL				7.391	62.956	50.781		64.81	8
	ATOM	5925	N	SER				9.511	62.177	50.738	1.00	64.05	7
20	ATOM	5926	CA	SER			5	9.824	62.684	52.072	1.00	64.03	6
	MOTA	5927	СВ	SER	D	126	6	1.317	62.517	52.362	1.00	63.15	6
	MOTA	5928	OG	SER	D	126	6	2.088	63.277	51.455	1.00	61.24	8
	MOTA	5929	C	SER			5	9.426	64.146	52.233	1.00	63.55	6
	ATOM	5930	0	SER	D	126		9.745	64.989	51.396	1.00	62.30	8
25	MOTA	5931	N	GLY				8.716	64.434	53.315		64.29	7
	MOTA	5932	CA	GLY				8.285	65.794	53.564		67.20	6
	MOTA	5933	C	GLY				6.868	66.085	53.115		68.64	6
	MOTA	5934	0	GLY				6.368	67.190	53.321		69.55	8
30	MOTA	5935	N	VAL				6.207	65.103	52.510		70.10	7
30	MOTA	5936	CA	VAL				4.845	65.323	52.038		71.31	6
	ATOM ATOM	5937 5938	CB CC1	VAL VAL				4.252	64.077 63.859	51.378 50.035		69.98 72.53	6 6
	ATOM	5939		VAL				4.476	62.877	52.271		70.16	6
	MOTA	5940	C	VAL				3.883	65.707	53.136		71.70	6
35	ATOM	5941	Ö	VAL				3.089	66.634	52.978		69.47	8
•	MOTA	5942	N	ASP				3.960	64.993	54.251		73.53	7
	ATOM	5943	CA	ASP				3.022	65.233	55.320		77.21	6
	ATOM	5944	CB.	ASP				3.171	64.197	56.428		78.32	6
	ATOM	5945	CG	ASP	D	129	5	1.860	63.985	57.204	1.00	80.24	6
40	ATOM	5946		ASP				1.521	62.805	57.509		81.78	8
	MOTA	5947	OD2	ASP	D	129		1.172	64.996	57.504		78.07	8
	MOTA	5948	С	ASP				3.027	66.618			79.33	6
	MOTA	5949	0	ASP				2.082	66.963	56.644		80.54	8
4 =	ATOM	5950	N	THR				4.041	67.433	55.604		80.13	7
45	ATOM	5951	CA	THR				4.048	68.779	56.171		80.39	6
	ATOM	5952	CB	THR				4.064	68.702	57.716		83.74	6
	ATOM ATOM	5953 5954		THR THR				4.418	67.359 69.136	58.114 58.320		84.65 81.78	8 6
	ATOM	5955	CGZ	THR				5.110	69.794	55.795		78.83	6
50	ATOM	5956	0	THR				6.241	69.440	55.449		77.71	8
•	ATOM	5957	N	GLU				4.701	71.065	55.921		78.93	7
	ATOM	5958	CA	GLU				5.520	72.272	55.705		78.30	6
	ATOM	5959	СВ	GLU				6.825	72.165	56.518		81.28	6
	ATOM	5960	CG	GLU				6.641	72.410	58.024		83.84	6
55	ATOM	5961	CD	GLU				7.696	71.715	58.856		84.29	6
	ATOM	5962		GLU				8.893	71.821	58.485		85.14	8
2	ATOM	5963		GLU				7.321	71.068	59.870		82.70	8
	ATOM	5964	С	GLU				5.869	72.672	54.295		75.98	6
60	MOTA	5965	0	GLU				5.047	73.205	53.552		74.51	8
60	ATOM	5966	N	SER				7.136	72.452	53.973		75.06	7
	MOTA	5967	CA	SER	.D	132	5	7.689	72.733	52.665	1.00	74.59	6

	WO 01/58	951							PCT/EP01/01	457
						-170				
	ATOM	5968	СВ	SER I	132	59.215	72.882	52.788	1.00 75.96	6
	ATOM	5969	OG	SER I		59.812	71.733	53.401	1.00 76.36	8
	MOTA	5970	C	SER I		57.316	71.551	51.753	1.00 72.89	6
	ATOM	5971	0	SER I	132	57.636	71.530	50.563	1.00 73.06	8
5	ATOM	5972	N	GLY I	133	56.630	70.575	52.337	1.00 70.56	7
	MOTA	5973	CA	GLY I	133	56.203	69.406	51.599	1.00 67.95	6
	ATOM	5974	С	GLY I		57.326	68.647	50.917	1.00 66.74	6
	ATOM	5975	0	GLY I		58.504	68.784	51.257	1.00 65.57	8
10	ATOM	5976	N	ALA I		56.950	67.830	49.942	1.00 65.62	7
10	ATOM	5977	CA	ALA I		57.922	67.052	49.194	1.00 63.00	6
	MOTA	5978	СВ	ALA I		57.506	65.586	49.145	1.00 62.05 1.00 60.69	6
	MOTA MOTA	5979 5980	С О	ALA I		58.060 57.215	67.597 68.357	47.785 47.298	1.00 50.69	6 8
	MOTA	5981	N	THR I		59.149	67.206	47.139	1.00 60.08	7
15	ATOM	5982	CA	THR I		59.417	67.619	45.777	1.00 59.14	6
	ATOM	5983	CB	THR I		60.585	68.590	45.703	1.00 59.67	6
	ATOM	5984		THR I		60.291	69.735	46.516	1.00 62.19	8
	ATOM	5985	CG2	THR I	135	60.811	69.031	44.263	1.00 57.77	6
	ATOM	5986	С	THR I		59.726	66.387	44.963	1.00 57.95	6
20	ATOM	5987	0	THR I	135	60.801	65.804	45.065	1.00 56.51	8
	ATOM	5988	N	CYS I		58.740	65.995	44.170	1.00 56.67	7
	ATOM	5989	CA	CYS I		58.825	64.836	43.314	1.00 55.02	6
	ATOM	5990	C	CYS I		59.172	65.310	41.906	1.00 55.53	6
25	ATOM	5991	0	CYS I		58.413	66.060	41.282	1.00 53.64	8
25	MOTA MOTA	5992 5993	CB	CYS I		57.475 57.280	64.115	43.347 42.175	1.00 55.35 1.00 52.04	6 16
	ATOM	5994	SG N	ARG I		60.331	62.756 64.889	41.414	1.00 52.04	7
	ATOM	5995	CA	ARG I		60.752	65.291	40.084	1.00 56.13	6
	ATOM	5996	СВ	ARG I		62.233	65.664	40.080	1.00 59.85	6
30	ATOM	5997	CG	ARG I		62.587	66.818	40.993	1.00 64.22	,6
	ATOM	5998	CD	ARG I		64.042	66.718	41.445	1.00 67.87	6
	MOTA	5999	NE	ARG I		64.261	67.425	42.706	1.00 72.81	7
	MOTA	6000	cz	ARG I	137	64.221	68.753	42.848	1.00 76.15	6
	MOTA	6001		ARG I		63.975	69.545	41.798	1.00 76.59	7
35	MOTA	6002		ARG I		64.408	69.295	44.051	1.00 75.96	7
•	MOTA	6003	C	ARG I		60.511	64.156	39.112	1.00 54.79	6
	ATOM	6004	0	ARG I		60.844	63.011	39.394	1.00 55.64	8
	MOTA	6005	N	ILE I		59.935	64,498	37.966	1.00 52.46	7
40	MOTA MOTA	6006 6007	CA CB	ILE I		59.618 58.092	63.551 63.516	36.923 36.686	1.00 49.86 1.00 47.60	· 6
70	MOTA	6008		ILE I		57.769	62.562	35.565	1.00 47.00	6
	MOTA	6009		ILE I		57.368	63.120	37.975	1.00 44.38	6
	MOTA	6010		ILE I		55.873	63.274	37.903	1.00 39.29	6
	ATOM	6011	C	ILE I		60.307	64.004	35.645	1.00 50.53	6
45	MOTA	6012	0	ILE I		60.056	65.103	35.163	1.00 47.86	8
	MOTA	6013	N	LYS I	139	61.171	63.158	35.093	1.00 52.17	7
	MOTA	6014	CA	LYS I		61.881	63.497	33.857	1.00 53.46	6
	MOTA	6015	CB	LYS 1		63.381	63.195	33.988	1.00 54.96	. 6
<b>50</b>	MOTA	6016	CG	LYS I		64.040	63.838	35.187	1.00 59.06	6
50	ATOM	6017	CD	LYS 1		65.558	63.761	35.119	1.00 60.55	6
	MOTA	6018	CE		139		64.685	34.044	1.00 62.84	6
	MOTA	6019	NZ	LYS I		67.604 61.335	64.584	33.930	1.00 64.96 1.00 52.45	7
	ATOM ATOM	6020 6021	С О	LYS I		.61.335 61.269	62.715 61.493	32.667 32.708	1.00 52.45	6 8
55	MOTA	6021	Ŋ	ILE I		60.953	63.411	31.604	1.00 52.48	7
	ATOM	6023	CA	ILE I		60.453	62.723	30.426	1.00 51.40	6
	MOTA	6024	СВ	ILE I		58.886.		30.369	1.00 52.71	6
	ATOM	6025		ILE I		58.303	62.478	31.748	1.00 53.74	6
	MOTA	6026		ILE I		58.387	64.171	30.003	1.00 52.18	6
60	MOTA	6027	CD1	ILE 1		56.892	64.354	30.322	1.00 51.22	6
	MOTA	6028	С	ILE 1	140	61.078	63.251	29.123	1.00 50.75	6

	WO 01/58	951							PCT	PCT/EP01/01457			
								-171					
	MOTA	6029	0	ILE				61.189	64.451	28.918		50.51	8
	MOTA	6030	N	GLY				61.511	62.340	28.258		48.91	7
	ATOM ATOM	6031 6032	CA C	GLY GLY				62.112 62.036	62.735 61.611	26.997		48.03	6 6
5	ATOM	6032	0	GLY				61.636	60.511	25.983 26.340		47.81 50.42	8
Ü	MOTA	6034	N	SER				62.405	61.865	24.729		45.08	7
	ATOM	6035	CA	SER				62.364	60.824	23.713		42.21	6
	ATOM	6036	СВ	SER				62.872	61.334	22.376		43.40	6
	MOTA	6037	OG	SER				63.079	60.255	21.482	1.00	43.21	8
10	MOTA	6038	С	SER	D	142		63.194	59.630	24.126	1.00	44.37	6
	MOTA	6039	0	SER				64.284	59.758	24.688	1.00	45.99	8
	MOTA	6040	N	TRP			•	62.673	58.452	23.825		46.12	7
	ATOM	6041	CA.	TRP				63.338	57.222	24.196		45.24	6
15	ATOM ATOM	6042 6043	CB CG	TRP TRP				62.300	56.121	24.425		42.93	6
10	ATOM	6043	CD2	TRP				62.872 63.244	54.893 54.737	25.051 26.418		39.90 37.42	6 6
	ATOM	6045	CE2	TRP				63.740	53.425	26.567		37.64	6
	ATOM	6046	CE3					63.204	55.581	27.536		35.75	6
	MOTA	6047	CD1					63.154	53.702	24.436		40.17	6
20	ATOM	6048	NE1	TRP	D	143		63.676	52.817	25.341	1.00	38.55	7
	MOTA	6049		TRP				64.187	52.935	27.788	1.00	38.02	6
	MOTA	6050	CZ3	TRP				63.647	55.100	28.741		36.62	6
	MOTA	6051	CH2	TRP				64.133	53.784	28.863		39.07	6
25	MOTA MOTA	6052 6053	C 0	TRP				64.348	56.758 56.109	23.170		46.24	6
25	ATOM	6054	N	TRP THR				65.328 64.124	57.080	23.509 21.910		48.11 45.62	8 7
	ATOM ·	6055	CA	THR				65.047	56.616	20.894		44.68	6
	ATOM	6056	CB	THR				64.336	55.633	19.955		44.87	6
	ATOM	6057	OG1	THR				63.155	56,242	19.421		41.93	8
30	ATOM	6058	CG2	THR	D	144		63.931	54.394	20.720	1.00	44.03	6
	ATOM	6059	С	THR				65.703	57.710	20.075		46.21	6
	ATOM	6060	0	THR		144		66.662	57.452	19.366		47.29	8
	ATOM	6061	N	HIS				65.198	58.931	20.173		47.13	7
35	MOTA MOTA	6062 6063	CA CB	HIS HIS				65.772 64.672	60.021	19.403 18.679		50.18	6
00	ATOM	6064	CG	HIS				63.961	60.793 59.997	17.630		52.45	6 6
	ATOM	6065		HIS				64.369	59.558	16.416		51.92	6
	ATOM	6066		HIS				62.652	59.589	17.765		50.59	7
	ATOM	6067	CE1	HIS	D	145		62.282	58.936	16.679	1.00	51.27	6
40	ATOM	6068	NE2	HIS	D	145		63.305	58.902	15.844	1.00	52.81	7
	ATOM	6069	С	HIS				66.611	60.990	20.241		52.96	6
	ATOM	6070	0	HIS				66.147	61.554	21.236		51.74	8
	ATOM	6071	N	HIS				67.856	61.179	19.828		53.81	7
45	MOTA MOTA	6072 6073	CA CB	HIS HIS				68.748 70.205	62.081 61.691	20.532		55.05 53.71	6
70	ATOM	6074	CG	HIS				70.203	61.617	20.267 18.816		52.77	6 6
	ATOM	6075		HIS				70.335	62.526	17.821		53.89	6
	ATOM	6076		HIS				71.083	60.487	18.236		49.45	7
	ATOM	6077		HIS				71.261	60.700	16.945	1.00	49.76	6
50	MOTA	6078	NE2	HIS	D	146		70.869	61.929	16.667	1.00	51.93	7
	ATOM	6079	C	HIS				68.489	63.521	20.094		56.51	6
	ATOM	6080	0	HIS				67.682	63.770	19.185		58.53	8
	MOTA	6081	N	SER				.69.190	64.455	20.738		57.97	7
55	MOTA MOTA	6082 6083	CA CB	SER SER				69.054 70.097	65.902 66.646	20.497 21.332		58.69 58.36	6 6
55	ATOM	6083	OG	SER				71.365	66.032	21.332		58.90	8
	ATOM	6085	C	SER				69.114	66.404	19.049		57.67	6
	ATOM	6086	Ō	SER				68.570	67.470	18.727		55.79	8
	ATOM	6087	N	ARG	D	148		69.768	65.647	18.180		57.54	7
60	MOTA	6088	CA	ARG				69.878	66.061	16.790		59.37	6
	MOTA	6089	CB	ARG	D	148		71.054	65.340	16.126	1.00	64.67	6

	WO 01/58	951							PCT/EP01/014	157
						-172				
	ATOM	6090	CG	ARG :	148	72.382	65.498	16.869	1.00 73.01	6
	MOTA	6091	CD	ARG 1	D 148	73.494	64.621	16.270	1.00 79.78	б
	ATOM	6092	NE	ARG 1	148	74.652	64.495	17.172	1.00 86.45	7
_	MOTA	6093	cz	ARG 1	148	75.435	65.508	17.558	1.00 88.85	6
5	ATOM	6094	NH1	ARG I		75.200	66.749	17.126	1.00 90.23	7
	MOTA	6095	NH2		D 148	76.462	65.284	18.381	1.00 89.74	7
	ATOM	6096	С		D 148	68.603	65.790	16.001	1.00 58.14	б
	ATOM	6097	0		D 148	68.406	66.351	14.921	1.00 57.28	8
10	ATOM	6098	N		D 149	67.737	64.932	16.546	1.00 58.44	7
10	ATOM	6099	CA		D 149	66.488	64.555	15.881	1.00 54.51	6
	ATOM	6100	CB		D 149	66.394	63.030	15.787	1.00 54.24	6
	MOTA MOTA	6101 6102	CG CD		D 149 D 149	67.744 67.687	62.384 60.886	15.474	1.00 56.46 1.00 57.56	6 6
	ATOM	6102	OE1		D 149	67.015	60.226	15.343 16.171	1.00 57.56	8
15	ATOM	6104	OE2		D 149	68.336	60.365	14.415	1.00 56.79	8
. •	ATOM	6105	C		D 149	65.315	65.123	16.638	1.00 51.56	6
	ATOM	6106	ō		D 149	64.396	65.667	16.050	1.00 48.50	8
	ATOM	6107	N		D 150	65.355	65.002	17.954	1.00 51.48	7
	MOTA	6108	CA	ILE :	D 150	64.284	65.533	18.783	1.00 53.11	6
20	ATOM	6109	CB		D 150	63.382	64.424	19.410	1.00 55.50	6
	ATOM	6110	CG2	ILE :	D 150	62.530	65.013	20.542	1.00 52.41	6
	MOTA	6111	CG1	ILE :	D 150	62.440	63.830	18.352	1.00 55.09	6
	MOTA	6112	CD1	ILE :	D 150	61.549	62.728	18.884	1.00 53.30	6
	ATOM	6113	С		D 150	64.841	66.339	19.925	1.00 54.06	6
25	MOTA	6114	0		D 150	65.809	65.944	20.573	1.00 49.46	8
	MOTA	6115	N		D 151	64.199	67.474	20.162	1.00 55.80	7
	ATOM	6116	CA		D 151	64.570	68.365	21.245	1.00 57.52	6
	ATOM	6117	CB		D 151	65.190	69.660	20.688	1.00 59.00	6
30	MOTA	6118	OG G		D 151	64.256	70.404	19.906	1.00 62.67	8
30	MOTA MOTA	6119 6120	C		D 151	63.269	68.663	21.989	1.00 57.81	6
	ATOM	6121	N O		D 151 D 152	62.241 63.315	68.932 68.592	21.373 23.312	1.00 55.28 1.00 59.48	8 7
	ATOM	6122	CA		D 152	62.142	68.851	23.312	1.00 59.48	6
	ATOM	6123	СВ		D 152	61.940	67.742	25.188	1.00 63.11	6
35	ATOM	6124	CG1		D 152	61.945	66.373	24.511	1.00 63.08	6
	ATOM	6125	CG2		D 152	63.038	67.821	26.259	1.00 61.64	6
	MOTA	6126	С	VAL :	D 152	62.350	70.167	24.854	1.00 63.67	6
	MOTA	6127	0	VAL	D 152	63.478	70.496	25.231	1.00 63.11	8
	MOTA	6128	N	ASP :	D 153	61.266	70.909	25.070	1.00 65.73	7
40	MOTA	6129	CA	ASP	D 153	61.365	72.206	25.740	1.00 68.62	6
	MOTA	6130	CB		D 153	61.524	73.296	24.680	1.00 70.73	6
	ATOM	6131	CG-		D 153	62.698	73.023	23.733	1.00 74.59	6
	MOTA	6132			D 153	63.854	73.332	24.118	1.00 73.93	8
45	MOTA	6133			D 153	62.473	72.483	22.612	1.00 76.61	8
40	MOTA	6134	C		D 153	60.144	72.513	26.601	1.00 69.92	6
	MOTA MOTA	6135 613 <i>6</i>	O N		D 153 D 154	59.022 60.345	72.176 73.139	26.227	1.00 71.07 1.00 71.13	8
	ATOM	6137	N CD		D 154	61.609	73.139	27.778 28.536	1.00 71.13	7 6
	MOTA	6138	CA		D 154	59.199	73.471	28.645	1.00 70.02	6
50	MOTA	6139	CB		D 154		73.882	29.955	1.00 71.74	6
	MOTA	6140	CG		D 154		73.062	29.962	1.00 70.60	6
	MOTA	6141	С		D 154	58.374	74.609	28.030	1.00 75.79	6
	ATOM	6142	0		D 154	.58.732	75.140	26.983	1.00 76.11	8
	MOTA	6143	N		D 155	57.286	75.001	28.686	1.00 80.37	7
55	MOTA	6144	CA		D 155	56.419	76.060	28.148	1.00 84.32	6
	MOTA	6145	CB		D 155	55.208	75.436	27.393°	1.00 84.09	6
	MOTA	6146	OG1		D 155	54.342	74.785	28.337	1.00 83.35	8
	MOTA	6147	CG2		D 155	55.685	74.412	26.360	1.00 83.23	6
60	MOTA	6148	C		D 155	55.861	77.068	29.184	1.00 88.09	6
60	MOTA	6149	0		D 155		77.366	30.211	1.00 88.59	8
	ATOM	6150	N	IHK	D 156	54.654	77.578	28.886	1.00 91.07	7

	WO 01/58	951								PCT/EP01/01	457
							-173				
	MOTA	6151	CA	THE	ח	156	53.911	78.559	29.705	1.00 93.25	6
	ATOM	6152	СВ			156	52.372	78.483	29.424	1.00 94.48	6
	MOTA	6153	OG1				52.115	78.686	28.019	1.00 94.94	8
	ATOM	6154	CG2				51.619	79.546	30.255	1.00 93.74	6
5	ATOM	6155	C			156	54.104	78.445	31.220	1.00 94.44	6
	ATOM	6156	0			156	53.471	77.615	31.898	1.00 93.56	8
	MOTA	6157	N			157	54.955	79.314	31.750	1.00 96.79	7
	ATOM	6158	CA			157	55.252	79.320	33.183	1.00 99.37	6
	ATOM	6159	CB	GLU	D	157	56.670	79.865	33.416	1.00100.34	6
10	ATOM	6160	CG	GLU	D	157	57.701	79.333	32.426	1.00102.84	6
	ATOM	6161	CD	GLU	D	157	59.086	79.955	32.629	1.00104.89	6
	MOTA	6162	OE1	GLU	D	157	59.179	81.213	32.700	1.00104.68	8
	MOTA	6163	OE2	GLU	D	157	60.085	79.189	32.707	1.00105.54	8
<i>-</i> -	MOTA	6164	С	GLU	D	157	54.237	80.165	33.967	1.00 99.49	6
15	MOTA	6165	0	GLU			54.273	80.216	35.210	1.00100.21	8
	MOTA	6166	N	ASN			53.336	80.828	33.248	1.00 98.56	7
	ATOM	6167	CA	ASN			52.340	81.657	33.911	1.00 98.16	6
	ATOM	6168	CB	ASN			51.632	82.550	32.894	1.00100.26	6
20	ATOM	6169	CG	ASN			52.610	83.378	32.064	1.00102.10	6
20	ATOM	6170		ASN			53.425	84.153	32.607	1.00101.77	8
	ATOM	6171		ASN			52.533	83.221	30.735	1.00102.21	7
	MOTA ATOM	6172 6173	C	ASN			51.313	80.786	34.613	1.00 96.52	6
	ATOM	6174	0	ASN SER			51.475	80.452	35.797	1.00 96.76	8
25	ATOM	6175	N CA	SER			50.257	80.447	33.864	1.00 94.02	7
2.0	ATOM	6176	CB	SER			49.142	79.599	34.313	1.00 90.18	6
	ATOM	6177	OG	SER			48.996 50.277	78.422	33.331	1.00 90.25	. 6
	ATOM	6178	C	SER			49.254	77.932 79.071	32.940 35.751	1.00 90.19	8
	ATOM	6179	Ö	SER			50.208	78.372	36.094	1.00 87.40 1.00 87.99	6
30	ATOM	6180	N	ASP			48.282	79.408	36.094	1.00 87.99	8 7
	ATOM	6181	CA	ASP			48.300	78.947	37.984	1.00 83.57	6
	ATOM	6182	СВ	ASP			46.950	79.189	38.660	1.00 79.26	6
	ATOM	6183	CG	ASP			46.902	78.632	40.079	1.00 79.02	6
	ATOM	6184	OD1	ASP			45.785	78.385	40.596	1.00 78.94	8
35	ATOM	6185		ASP			47.987	78.446	40.679	1.00 77.43	8
	ATOM	6186	С	ASP	D	160	48.579	77.453	37.995	1.00 77.55	6
	ATOM	6187	0 -	ASP	D	160	47.797	76.670	37.429	1.00 77.70	8
	ATOM	6188	N	ASP	D	161	49.676	77.062	38.646	1.00 74.02	7
	MOTA	6189	CA	ASP		_	50.070	75.657	38.719	1.00 69.51	6
40	ATOM	6190	CB	ASP			51.277	75.466	39.642	1.00 68.24	6
	MOTA	6191	CG	ASP			52.556	76.004	39.050	1.00 67.15	6
	MOTA	6192		ASP			52.734	75.886	37.827	1.00 67.47	8
	ATOM	6193		ASP			53.397	76.536	39.803	1.00 70.25	8
45	MOTA	6194	C	ASP			48.972	74.697	39.147	1.00 67.31	6
40	MOTA	6195	0	ASP			49.071	73.497	38.890	1.00 68.61	8
	ATOM ATOM	6196 6197	N	SER			47.924	75.191	39.788	1.00 64.39	7
	ATOM	6198	CA CB	SER SER			46.871	74.280	40.210	1.00 63.54	6
	ATOM	6199	OG	SER			46.897 46.555	74.097	41.736	1.00 63.26	6
50	ATOM	6200	C	SER			45.494	75.286 74.722	42.417 39.761	1.00 65.64 1.00 62.73	8
••	ATOM	6201	Ö	SER			44.490	74.439	40.425	1.00 62.73	6
	ATOM	6202	N	GLU			45.435	75.400	38.620	1.00 63.28	8
		6203	CA	GLU			44.149	75.861	38.139	1.00 66.60	7 6
	ATOM	6204	СВ	GLU			44.325	76.984	37.105	1.00 69.72	6
55	ATOM	6205	CG	GLU			44.576	76.546	35.681	1.00 03.72	6
	ATOM	6206	CD	GLU			44.506	77.720	34.698	1.00 74.42	6
	MOTA	6207		GLU			45.442	78.557		1.00 75.59	8
	ATOM	6208	OE2	GLU			43.510	77.808	33.932	1.00 73.89	8
	ATOM	6209	С	GLU			43.310	74.712	37.572	1.00 65.25	6
60	ATOM	6210	0	GLU			42.126	74.885	37.264	1.00 65.73	8
	MOTA	6211	N	TYR	D	164	43.926	73.539	37.448	1.00 64.10	7

	WO 01/58								PCT	<b>EP</b> 01/01	457	
							-174					
	ATOM	6212	CA	TYR	D 16	Λ	43.236	72.353	36.946	1 00	61.14	c
	ATOM	6213	CB	TYR			43.236	71.828	35.675			6
	ATOM	6214	CG	TYR			43.794	72,756			62.34	6
	ATOM	6215	CD1				44.937		34.501		62.07	6
5	ATOM	6216		TYR				73.264 74.152	33.887		62.29	6
J	ATOM	6217		TYR			44.846		32.813		64.14	6
	ATOM	6218					42.547	73.151	34.016		63.36	6
	ATOM	6219	CE2	TYR TYR			42.438	74.038	32.940		65.18	6
	ATOM	6220	CZ				43.594	74.536	32.337		65.18	6
10	ATOM	6221	C , OH	TYR TYR			43.495	75.380	31.240		65.32	8
10	ATOM	6222					43.257	71.263	38.000		59.77	6
	ATOM	6223	0	TYR			42.602	70.231	37.853		59.16	8
	ATOM	6224	N	PHE			44.008	71.497	39.068		57.70	7
			CA	PHE			44.113	70.518	40.143		56.00	6
15	ATOM	6225	CB	PHE			45.105	70.988	41.202		53.27	6
10	ATOM	6226	CG	PHE			45.635	69.885	42.053		51.93	6
	MOTA	6227	CD1				46.436	68.891	41.502		50.62	6
	MOTA	6228	CD2				45.326	69.820	43.398		52.41	6
	MOTA	6229		PHE			46.922	67.845	42.283		49.13	6
20	ATOM	6230		PHE			45.807	68.777	44.188		52.20	6
20	MOTA	6231	CZ	PHE			46.608	67.788	43.624		51.98	6
	MOTA	6232	С	PHE			42.773	70.241	40.801		55.90	6
	ATOM	6233	0	PHE			41.970	71.149	41.005		56.82	8
	MOTA	6234	N	SER			42.524	68.980	41.126		55.56	7
25	ATOM	6235	CA	SER			41.273	68.627	41.771		55.90	6
20	ATOM	6236	CB	SER			41.115	67.117	41.887		55.69	- 6
	ATOM	6237	OG	SER			39.855	66.799	42.457		55.69	8
	ATOM	6238	C	SER			41.280	69.229	43.158		56.73	6
	ATOM	6239	0	SER			42.315	69.229	43.839		56.74	8
30	MOTA	6240	N	GLN			40.121	69.729	43.578		57.58	7
30	ATOM	6241	CA	GLN			39.999	70.353	44.892		57.81	6
	ATOM	6242	CB	GLN			38.867	71.383	44.885		59.24	6
	MOTA	6243	CG	GLN			37.541	70.794	44.439		63.59	6
	ATOM	6244	CD	GLN			36.485	71.854	44.107		65.57	6
35	ATOM	6245		GLN			36.054	72.607	44.979		65.98	8
33	MOTA	6246	NE2				36.067	71.909	42.831		65.54	7
	ATOM	6247	C	GLN :			39.752	69.328	45.977		56.65	6
	ATOM	6248	0	GLN			39.990	69.598	47.151		56.95	8
	ATOM	6249	N	TYR :			39.293	68.145	45.586		56.16	7
40	ATOM	6250	CA	TYR :			39.014	67.091	46.556		53.65	6
40.	MOTA	6251	CB	TYR :			37.798	66.297	46.096		54.14	6
	MOTA	6252	CG	TYR :		_	36.675	67.217	45.707		53.82	6
	ATOM	6253		TYR			36.446	67.545	44.371		53.19	. 6
	ATOM ATOM	6254	CD2	TYR :			35.445	68.454	44.020		54.20	6
45		6255					35.880	67.816	46.681		52.39	6
70	MOTA	6256		TYR :			34.881	68.722	46.342		52.03	6
	ATOM ATOM	6257 6258	CZ OH	TYR :			34.670	69.035	45.016		53.04	6
	ATOM			TYR :			33.683	69.917	44.689		53.97	8
		6259	C	TYR I			40.181	66.162	46.851		52.39	6
50	ATOM ATOM	6260 6261	0	TYR I			40.025	65.185	47.575		53.02	8
00	ATOM	6262	N	SER I			41.347	66.479	46.299		51.48	7
			CA	SER I			42.543	65.686	46.513		51.84	6
	MOTA	6263	CB	SER I			43.664	66.151	45.584		52.14	6
	ATOM ATOM	6264 6265	OG OG	SER I			44.878	65.483	45.881		50.95	8
55	ATOM	6266	0	SER I			43.001	65.828	47.953		53.72	6
	ATOM	6267	N	ARG 1			42.832 43.583	66.880	48.570		51.67	8
	ATOM	6268	CA	ARG I				64.761	48.487		54.84	7
	ATOM	6269	CB	ARG I			44.079	64.778	49.850		54.97	6
	ATOM	6270	CG	ARG I			44.460	63.366	50.297		54.29	6
60	ATOM	6270	CD	ARG I			43.369 43.436	62.647 61.124	51.081 50.955		57.60	6
- •	ATOM	6272	NE	ARG I			44.726	60.543	51.323		58.91 61,45	6
		4		1	1	-	44.140	00.543	J J4J	1.00	J. 43	7

	WO 01/58				100					PCT/EP01/01457				
		60.50			_	4.70		-175					<i>-</i> 1	_
	ATOM	6273 6274	CZ	ARG ARG				15.504 15.140		59.853	50.483		64.08 60.98	6 7
	MOTA ATOM	6275		ARG				16.649		59.656 59.334	49.220 50.906		64.65	7
	ATOM	6276	C	ARG				15.293		55.683	49.928		56.57	6
5	ATOM	6277	Ö	ARG				15.719		56.078	51.022		59.46	8
•	ATOM	6278	N	PHE				45.842		56.033	48.770		55.26	7
	MOTA	6279	CA	PHE				17.034		66.864	48.739		54.09	6
	MOTA	6280	CB	PHE	D	171	4	48.172	. 6	66.094	48.070	1.00	53.61	6
	MOTA	6281	CG	PHE				48.319		54.688	48.585		54.38	6
10	ATOM	6282		PHE				17.427		53.698	48.191		55.63	6
	ATOM	6283		PHE				49.315		54.364	49.498		54.14	6
	ATOM	6284		PHE				47.521		52.415	48.694		54.27	6
	ATOM	6285		PHE				19.414		53.078	50.008		54.92	6
15	ATOM ATOM	6286 6287	CZ C	PHE				48.516 46.821		52.103 58.195	49.605 48.049		54.58 53.25	6 6
10	ATOM	6288	0	PHE				45.759		58.457	47.500		52.23	8
	MOTA	6289	N	GLU				17.836		59.045	48.100		52.75	7
	ATOM	6290	CA	GLU				47.741		70.347	47.479		55.31	6
	ATOM	6291	CB	GLU	D	172	4	47.327		71.413	48.505	1.00	58.80	. 6
20	MOTA	6292	CG	GLU	D	172	4	48.293	-	71.616	49.686	1.00	62.32	6
	MOTA	6293	CD	GLU				47.773		72.633	50.693		64.33	6
	MOTA	6294		CLU				47.132		73.617	50.251		64.06	8
	MOTA	6295		GLU				48.012		72.456	51.915		65.29	8
25	MOTA	6296	C	GLU				49.083		70.671	46.861		56.32	6
20	ATOM ATOM	6297 6298	0 N	GLU				50.115 49.063		70.122 71.550	47.265 45.864		54.59 56.82	8 7
	ATOM	6299	N CA	ILE				50.286		71.330	45.864		57.96	6
	ATOM	6300	CB	ILE				50.062		72.033	43.171		57.06	. 6
	ATOM	6301		ILE				51.332		72.535	42.959		56.84	. 6
30	MOTA	6302		ILE				19.663		70.675	43.080		55.34	6
	ATOM	6303	CD1				4	49.371		70.720	41.622	1.00	53.59	6
	ATOM	6304	С	ILE	D	173		50.848	-	73.250	45.653	1.00	59.20	6
	MOTA	6305	0	ILE				50.132		74.249	45.756		58.03	8
05	ATOM	6306	N	LEU				52.140		73.251	45.949		60.22	7
35	ATOM	6307	CA	LEU				52.784		74.473	46.394		61.88	6
	ATOM	6308 6309	CB CG	LEU				53.929		74.136	47.340		61.02	6
	ATOM ATOM	6310		LEU				53.512 54.722		73.196 72.881	48.469 49.330		61.46 62.06	· 6
	ATOM	6311		LEU				52.395		73.823	49.284		59.37	6
40	ATOM	6312	C	LEU				53.302		75.193	45.151		63.17	6
	ATOM	6313	Ō	LEU				52.979		76.357	44.899		63.68	8
	ATOM	6314	N	ASP				54.080	-	74.479	44.349	1.00	64.58	7
	MOTA	6315	CA	ASP			į	54.627	•	75.067	43.145		65.97	6
4 =	ATOM	6316	CB	ASP				55.789		75.993	43.538		67.34	6
45	ATOM	6317	CG	ASP				56.390		76.748	42.354		69.43	6
	ATOM	6318		ASP				55.636		77.413	41.584		69.68	8
	ATOM ATOM	6319 6320	C C	ASP ASP				57.635 55.085		76.685 73.984	42.214 42.164		69.28 66.38	8
	ATOM	6321	0	ASP				55.380		72.846	42.561		66.58	6 8
50	ATOM	6322		VAL				55.118		74.342	40.881		65.75	7
	ATOM	6323	CA	VAL				55.536		73.436	39.831		65.19	6
	ATOM	6324	CB	VAL				54.330		72.945	38.992		64.89	6
	ATOM	6325	CG1	VAL	D	176		54.818		72.085	37.811		64.67	6
	MOTA	6326		VAL				53.382		72.145	39.865		65.95	6
55	ATOM	6327	C	VAL				56.477		74.190	38.919		66.36	6
	ATOM	6328	0	VAL				56.178		75.314	38.513		66.32	8
	ATOM	6329	N	THR				57.614		73.576	38.602		68.04	7
	ATOM ATOM	6330 6331	CA CB	THR				58.598 59.763		74.184 74.819	37.708		69.05 67.62	6
60	ATOM	6332		THR				60.349		73.843	38.496 39.370		63.42	6 8
- <b>-</b>	ATOM	6333		THR				59.258		76.013	39.305		66.11	6

	WO 01/58	8951							PCT/EP01/014	157
						-176				
	MOTA	6334	С		177	59.165	73.144	36.739	1.00 71.66	6
	MOTA	6335	0		177	59.373	71.973	37.111	1.00 73.56	8
	ATOM	6336	N		178	59.417	73.568	35.501	1.00 71.95	7
c	ATOM	6337	CA	GLN I		59.941	72.667	34.488	1.00 72.06	6
5	MOTA	6338	CB	GLN I		58.932	72.511	33.347	1.00 74.14	6
	ATOM	6339	CG	-	178	57.466	72.700	33.754	1.00 76.97	6
	ATOM ATOM	6340 6341	CD OE1		178	56.497 56.603	72.041 72.230	32.772 31.551	1.00 78.22 1.00 79.44	6 8
	ATOM	6342	NE2	GLN I		55.544	71.266	33.302	1.00 75.44	7
10	MOTA	6343	C		178	61.219	73.240	33.936	1.00 70.70	6
	ATOM	6344	Ö	-	178	61.226	74.368	33.462	1.00 71.24	8
	MOTA	6345	N	LYS I		62.291	72.461	33.979	1.00 71.70	7
	ATOM	6346	CA		179	63.593	72.904	33.474	1.00 71.59	6
	ATOM	6347	CB	LYS I	179	64.553	73.170	34.642	1.00 73.63	6
15	ATOM	6348	CG	LYS I	179	63.906	73.953	35.800	1.00 77.80	6
	ATOM	6349	CD	LYS 1	179	64.795	74.018	37.040	1.00 78.53	6
	MOTA	6350	CE		179	64.016	74.470	38.273	1.00 79.16	6
	ATOM	6351	NZ		D 179	62.899	73.537	38.610	1.00 77.90	7
00	ATOM	6352	С	LYS I		64.173	71.807	32,601	1.00 70.50	6
20	ATOM	6353	0	LYS I		64.549	70.754	33.112	1.00 69.32	8
	MOTA	6354	N	LYS I		64.252	72.044	31.294	1.00 69.56	7
	MOTA MOTA	6355 6356	CA CB		180 180	64.803 64.581	71.039 71.464	30.382	1.00 69.55 1.00 69.05	6 6
	ATOM	6357	CG		180	65.462	72.584	28.419	1.00 69.05	6
25	ATOM	6358	CD		D 180	66.773	72.041	27.860	1.00 66.86	6
	ATOM	6359	CE	LYS I		66.550	71.200	26.619	1.00 63.97	6
	ATOM	6360	NZ		180	66.096	72,020	25.476	1.00 64.54	7
	ATOM	6361	C		180	66.293	70.795	30.642	1.00 68.87	6
	ATOM	6362	0	LYS I	180	66.869	71.406	31.536	1.00 69.83	8
30	MOTA	6363	N	ASN I	181	66.905	69.879	29.897	1.00 68.37	7
	MOTA	6364	CA	ASN I	181	68.326	69.615	30.060	1.00 70.05	6
	ATOM	6365	CB	ASN I		68.711	69.461	31.540	1.00 70.86	6
	MOTA	6366	CG	ASN I		67.808	68.533	32.291	1.00 71.68	6
35	ATOM	6367		ASN I		67.498	67.446	31.823	1.00 74.38	8
33	MOTA	6368		ASN I		67.395	68.945	33.487	1.00 72.61	7
	ATOM ATOM	6369 6370	C		D 181	68.905	68.449	29.281	1.00 70.12 1.00 68.91	6
	ATOM	6371	N O		182	68.535 69.844	67.303 68.760	29.491 28.385	1.00 68.91	8 7
	ATOM	6372	CA		182	70.519	67.744	27.577	1.00 71.81	6
40	ATOM	6373	СВ		182	71.361	68.418	26.495	1.00 70.60	6
	ATOM	6374	OG		182	71.817	67.463	25.557	1.00 71.86	8
•	ATOM	6375	С		182	71.405	66.866	28.482	1.00 71.03	6
	MOTA	6376	0	SER 1	D 182	71.794	67.281	29.572	1.00 72.13	8
	ATOM	6377	N	VAL I	D 183	71.715	65.653	28.037	1.00 70.45	7
45	ATOM	6378	CA		183	72.528	64.736	28.842	1.00 69.61	6
	MOTA	6379	CB		D 183	71.728	64.221	30.066	1.00 69.93	6
	ATOM	6380		VAL 1		70.268	63.988	29.671	1.00 71.71	6
	ATOM	6381		VAL I		. 72.331	62.909	30.584	1.00 68.31	6
50	MOTA	6382	C		D 183	73.046	63.521	28.069	1.00 69.82	6
50	ATOM ATOM	6383 6384	O N		D 183	72.317 74.314	62.887 63 <i>.</i> 194	27.305 28.272	1.00 69.28 1.00 71.03	8 7
	ATOM	6385	CA		D 184	74.898	62.041	27.596	1.00 71.03	6
	ATOM	6386	CB		D 184	76.314	62.360	27.027	1.00 71.67	6
	ATOM	6387		THR		76.207	63.364	26.010	1.00 69.65	. 8
55	ATOM	6388		THR		76.944	61.110	26.404	1.00 71.24	6
	ATOM	6389	C		D 184	74.997	60.901	28.602	1.00 73.76	6
	ATOM	6390	0	THR I	D 184	75.273	61.132	29.786	1.00 74.26	8
	ATOM	6391	N		D 185	74.749	59.679	28.139	1.00 74.82	7
00	ATOM	6392	CA		D 185	74.818	58.515	29.024	1.00 76.20	6
60	ATOM	6393	СВ		D 185	73.477	57.755	29.046	1.00 77.17	6
	ATOM	6394	CG	TYR I	D 185	72.286	58.637	29.324	1.00 77.03	6

	WO 01/58	8951							PCT/EP01/01	457
						-177				
	» mom	6395	an1	TYR I	105	71.822	59.527	28.362	1.00 77.16	6
	ATOM ATOM	6396		TYR I		70.781	60.416	28.640	1.00 78.65	6
	ATOM	6397		TYR I		71.676	58.643	30.578	1.00 78.44	6
	ATOM	6398		TYR I		70.629	59.532	30.873	1.00 78.76	6
5	ATOM	6399	CZ	TYR I		70.190	60.417	29.897	1.00 78.44	6
_	ATOM	6400	ОН	TYR I		69.173	61.311	30.160	1.00 78.64	8
	ATOM	6401	C	TYR I		75.909	57.595	28.525	1.00 76.37	6
	MOTA	6402	0	TYR I	185	76.062	57.403	27.320	1.00 75.86	8
	MOTA	6403	N	SER I	186	76.669	57.031	29.454	1.00 78.41	7
10	MOTA	6404	CA	SER I		77.762	56.127	29.097	1.00 80.47	6
	ATOM	6405	CB	SER I		78.353	55.494	30.361	1.00 80.37	6
	ATOM	6406	OG	SER I		77.324	55.000	31.202	1.00 80.82	8
	ATOM	6407	C	SER I		. 77.259	55.042	28.139 27.205	1.00 81.49 1.00 80.86	6 8
15	ATOM	6408	0	SER I		77.977 76.018	54.637 54.601	28.370	1.00 80.88	7
13	ATOM ATOM	6409 6410	N CA	CYS I		75.366	53.573	27.553	1.00 82.11	6
	ATOM	6411	C	CYS I		75.259	54.005	26.123	1.00 82.74	6
	ATOM	6412	Ö	CYS I		75.445	53.226	25.179	1.00 81.67	8
	ATOM	6413	СВ	CYS I		73.908	53.360	27.980	1.00 82.28	6
20	ATOM	6414	SG	CYS I		72.725	54.778	27.707	1.00 81.64	16
	ATOM	6415	N	CYS I		74.954	55.287	25.990	1.00 83.43	7
	ATOM	6416	CA	CYS I	188	74.614	55.827	24.701	1.00 83.03	6
	ATOM	6417	C	CYS I	188	75.379	57.070	24.204	1.00 81.94	6
	MOTA	6418	0	CYS I		75.401	58.127	24.860	1.00 81.77	8
25	MOTA	6419	CB	CYS I		73.091	56.059	24.777	1.00 83.56	6
	ATOM	6420	SG	CYS I		72.115	54.783	25.740	1.00 85.15	16
	MOTA	6421	N	PRO I		76.000	56.945	23.013	1.00 80.60	7
	MOTA	6422	CD.	PRO I		75.862	55.676	22.263	1.00 80.05 1.00 78.99	6
20	ATOM	6423	CA	PRO I		76.809	57.921 57.341	22.254 20.836	1.00 78.39	6 6
30	ATOM	6424	CB CG	PRO I	189	76.804 76.835	55.852	21.097	1.00 79.15	6
	ATOM ATOM	6425 6426	C		189	76.335	59.408	22.258	1.00 76.71	. 6
	ATOM	6427	0	PRO I		77.106	60.265	22.777	1.00 76.06	8
	ATOM	6428	N		190	75.237	59,713	21.663	1.00 73.54	7
35	ATOM	6429	CA		190	74.762	61,101	21.583	1.00 70.67	6
	ATOM	6430	CB		190	73.735	61.233	20.462	1.00 72.95	6
	ATOM	6431	CG	GLU I	190	73.941	60.272	19.292	1.00 76.22	6
	ATOM	6432	CD	GLU I	190	74.959	60.778	18.284	1.00 77.17	6
	ATOM	6433	OE1	GLU I		74.920	61.987	17.949	1.00 75.78	8
40	MOTA	6434	OE2			75.786	59.961	17.819	1.00 78.06	8
	ATOM	6435	С		D 190	74.113	61.576	22.874	1.00 67.13	6
	ATOM	6436			D 190	74.060	60.842	23.861	1.00 66.77	8
	MOŤA	6437	N		D 191	73.595	62.797	22.852	1.00 63.73 1.00 63.96	7 6
45	ATOM	6438	CA		D 191 D 191	72.924	63.362 64.833	24.027 24.188	1.00 63.96	6
40	ATOM ATOM	6439 6440	CB C		D 191	71.398	63.226	23.935	1.00 63.09	6
	ATOM	6441	0		D 191	70.824	63.324	22.848	1.00 63.27	8
	ATOM	6442	Ŋ		D 192	70.737	63.015	25.073	1.00 61.86	7
	ATOM	6443	CA		D 192	69.284	62.883	25.077	1.00 60.02	6
50	MOTA	6444	CB		D 192	68.874	61.483	25.544	1.00 58.87	6
	ATOM	6445	CG		D 192	69.185	60.408	24.531	1.00 59.77	6
	MOTA	6446	CD1	TYR	D 192	70.447	59.804	24.491	1.00 59.82	6
	ATOM	6447		TYR		70.762	58.849	23.514	1.00 59.91	6
	ATOM	6448		TYR		68.234	60.030	23.568	1.00 59.23	6
55	ATOM	6449		TYR		68.534	59.084	22.592	1.00 60.37	6
	ATOM	6450	CZ		D 192	69.803	58.496	22.566	1.00 61.99	6
	ATOM	6451	OH		D 192	70.120	57.582	21.581	1.00 61.54 1.00 59.37	8
	ATOM	6452	C		D 192	68.590 68.594	63.938 63.874	25.922 27.150	1.00 59.37	6 8
60	ATOM ATOM	6453 6454	O N		D 192 D 193	67.986	64.909	25.248	1.00 59.03	7
50	ATOM	6455	CA		D 193	67.280	65.992	25.915	1.00 60.46	6
	ATOR	2423	CA			0,1200				Ū

	WO 01/58	8951								PCT	<b>/EP01/0</b> 1	1457
	•						-178					
	АТОМ	6456	СВ	GLU :	n	193	66.832	67.054	24.898	1.00	61.02	6
	ATOM	6457	CG	GLU :			67.985	67.781	24.196		65.53	6
	ATOM	6458	CD	GLU :			67.522	68.937	23.292		66.58	6
	ATOM	6459		GLU			66.678	69.760	23.739		66.15	8
5	ATOM	6460	OE2	GLU			68.017	69.023	22.138		66.88	8
	ATOM	6461	С	GLU	D	193	66.066	65.455	26.658	1.00	61.32	· 6
	ATOM	6462	0	GLU	D	193	65.498	64.428	26.278	1.00	61.10	8
	ATOM	6463	N.	ASP	D	194	65.682	66.157	27.724		62.11	7
	ATOM	6464	CA	ASP			64.533	65.788	28.537		60.32	6
10	MOTA	6465	CB	ASP			64.855	64.571	29.416		60.68	6.
	MOTA	6466	CG	ASP			65.759	64.907	30.589		61.25	6
	MOTA	6467		ASP			66.929	64.453	30.591		62.58 61.10	8 8
	MOTA	6468	C C	ASP ASP			65.297 64.086	65.619 66.951	31.509 29.417		59.85	6
15	ATOM ATOM	6469 6470	0	ASP			64.890	67.793	29.816		60.03	8
10	ATOM	6471	N	VAL			62.792	66.993	29.704		57.38	7
	MOTA	6472	CA	VAL			62.225	68.024	30.538		55.36	6
	MOTA	6473	CB	VAL			60.864	68.480	30.001		52.24	6
	ATOM	6474	CG1	VAL	D	195	60.179	69.394	31.001	1.00	51.69	6
20	ATOM	6475	CG2	VAL	D	195	61.058	69.189	28.693		52.14	6
	MOTA	6476	С	VAL			62.044	67.460	31.935		56.36	6
	ATOM	6477	0	VAL			61.452	66.412	32.114		57.76	8
	ATOM	6478	N	GLU			62.571	68.151	32.930		58.67	7
0.5	ATOM	6479	CA	GLU			62.425	67.712	34.303		58.26	6
25	MOTA	6480	CB	GLU			63.754 63.725	67.833	35.035 36.460		58.61 61.95	6 6
	ATOM ATOM	6481 6482	CD	GLU			65.062	67.326 67.533	37.172		63.50	6
	ATOM	6483		GLU			66.083	67.014	36.679		62.21	8
	ATOM	6484	OE2	GLU			65.099	68.218	38.222		65.74	8
30	ATOM	6485	С	GLU			61.370	68.598	34.959	1.00	58.08	6
	ATOM	6486	0	GLU	D	196	61.500	69.822	34.997		59.87	8
	ATOM	6487	N	VAL			60.305	67.979	35.452		57.22	7
	ATOM	6488	CA	VAL			59.242	68.721	36.104		54.36	6
0.	MOTA	6489	CB	VAL			57.863	68.304	35.567		52.68	6
35	ATOM	6490		VAL VAL			56.772 57.809	69.095 68.517	36.255 34.068		49.60 50.84	6 6
	ATOM ATOM	6491 6492	CG2 C	VAL			59.317	68.420	37.587		55.10	6
	ATOM	6493	0	VAL			59.367	67.264	37.995		55.27	8
	ATOM	6494	N	SER			59.351	69,467	38.399		56.68	7
40	ATOM	6495	CA	SER			59.413	69.284	39.839	1.00	56.39	6
	ATOM	6496	CB	SER	D	198	60.487	70.188	40.448		55.89	6
	ATOM	6497	OG	SER			61.789	69.767	40.066		57.83	8
	MOTA	6498	С	SER			58.058	69.593	40.448		56.61	6
4=	ATOM	6499	0	SER			57.536	70.698	40.317		56.25	8
45	ATOM	6500	N	LEU			57.481	68.597 68.770	41.101		56.92 56.84	7 6
	ATOM	6501 6502	CA CB	LEU			56.189 55.303	67.561	41.728 41.468		57.08	6
	ATOM ATOM	6503	CG	LEU			53.981	67.553	42.243		57.99	,6
	ATOM	6504		LEU			53.094	68.726	41.834		57.12	6
50	ATOM	6505		LEU			53.272	66.246	41.971	1.00	58.22	6
	ATOM	6506	С	LEU	D	199	56.354	68.953	43.220	-	57.85	6
	MOTA	6507	0	LEU			56.625	67.998	43.950		58.46	8
	ATOM	6508	N	ASN			56.207	70.192	43.671		58.52	7
EE	MOTA	6509	CA	ASN			56.315	70.486	45.084		57.07 59.47	6
55	ATOM	6510 6511	CB CG	ASN ASN			57.017 57.126	71.827 72.184	45.311 46.781		59.47 61.26	6 6
	MOTA MOTA	6511 6512		ASN			57.508	71.359	47.613		60.78	8
	ATOM	6513		ASN			56.792	73.423	47.108		63.13	7
	ATOM	6514	C	ASN			54.886	70.533	45.593		.55.28	6
60	ATOM	6515	0	ASN	D	200	54.108	71.422	45.242		53.93	8
	MOTA	6516	N	PHE	D	201	54.549	69.554	46.419	1.00	53.26	7

	WO 01/58	951								PCT/EP01/0	1457
							-179				
	3 mO34	CE 1 7	<b>~</b> 3	Diffe	<b>.</b>	201	53.218	69.444	46.973	1.00 51.91	6
	ATOM	6517 6518	CA	PHE PHE			52.408	68.434	46.168	1.00 31.91	
	ATOM ATOM	6519	CB CG	PHE			52.870	67.013	46.348	1.00 46.59	
	ATOM	6520		PHE			52.068	66.086	47.003	1.00 45.61	
5	ATOM	6521		PHE			54.133	66.613	45.903	1.00 46.86	
5	ATOM	6522		PHE			52.519	64.779	47.218	1.00 45.68	
	ATOM	6523		PHE			54.597	65.312	46.112	1.00 44.48	
	ATOM	6524	CZ	PHE			53.788	64.394	46.772	1.00 44.43	
	ATOM	6525	C	PHE			53.760	68.940	48.386	1.00 53.35	
10	ATOM	6526	ō	PHE			54.456	68.570	48.818	1.00 52.18	
	ATOM	6527	N	ARG			52.238	68.902	49.093	1.00 55.22	
	ATOM	6528	CA	ARG			52.211	68.426	50.470	1.00 57.74	
	ATOM	6529	CB	ARG			52.632	69.546	51.412	1.00 58.53	
	ATOM	6530	CG	ARG			51.564	70.612	51.484	1.00 62.76	
15	ATOM	6531	CD	ARG			51.956	71,797	52.313	1.00 64.76	
	ATOM	6532	NE	ARG			50.901	72.806	52.296	1.00 64.52	
	ATOM	6533	CZ	ARG			51.046	74.035	52.779	1.00 65.00	
	ATOM	6534	NH1	ARG			52.206	74.409	53.323	1.00 65.86	
	MOTA	6535		ARG			50.045	74.896	52.708	1.00 62.46	7
20	ATOM	6536	С	ARG			50.788	67.997	50.835	1.00 57.64	. 6
	ATOM	6537	0	ARG	D :	202	49.822	68.392	50.186	1.00 55.63	8
	ATOM	6538	N	LYS	D :	203	50.668	67.189	51.878	1.00 58.55	7
	MOTA	6539	CA	LYS	D.	203	49.359	66.759	52.332	1.00 59.55	6
	MOTA	6540	CB	LYS	D :	203	49:505	65.708	53.428	1.00 60.97	6
25	MOTA	6541	CG	LYS	D	203	48.195	65.258	54.031	1.00 62.61	. 6
•	MOTA	6542	CD	LYS	D	203	48.445	64.319	55.194	1.00 66.11	. 6
	MOTA	6543	CE	LYS	D	203	47.142	63,813	55.784	1.00 68.33	
	MOTA	6544	NZ	LYS			46.380	62.985	54.804	1.00 69.98	
	MOTA	6545	С	LYS			48.702	68.008	52.914	1.00 60.27	
30	MOTA	6546	0	LYS			49.402	68,886	53.428	1.00 60.55	
	MOTA	6547	N	LYS			47.374	68.105	52.832	1.00 59.32	
	MOTA	6548	CA	LYS			46.680	69.260	53.395	1.00 60.40	
	MOTA	6549	CB	LYS			45.221	69.284	52.947	1.00 59.66	
ÒE	MOTA	6550	CG	LYS			45.054	69.738	51.495	1.00 56.15	
35	ATOM	6551	CD	LYS			43.652	69.489	50.974	1.00 52.10	
	MOTA	6552	CE	LYS			43.593	69.775	49.488	1.00 52.88	
	MOTA	6553	NZ	LYS			42.334	69.320	48.856	1.00 54.65 1.00 62.27	
	MOTA	6554	C	LYS			46.776	69.201	54.919	1.00 62.27	
40	MOTA	6555 6556	N O	LYS GLY			47.031	68.129	55.479 55.587	1.00 63.85	
70	MOTA	6557	CA	GLY			46.590 46.701	70.344 70.390		1.00 61.76	
	ATOM ATOM	6558	CA	GLY			45.432	70.390	57.821	1.00 60.96	
	ATOM	6559		GLY			44.364	70.704	57.191	1.00 61.45	
	ATOM	6560		GLY			45.495	70.835	59.067	1.00 60.53	
45	ATOM	6561	CB	PHE		1	68.481	57.493	1.362	1.00 63.85	
	ATOM	6562	CG	PHE		1	68.496	56.384	0.357	1.00 65.93	
	ATOM	6563		PHE		1	67.431	56.207	-0.526	1.00 67.13	
	ATOM	6564		PHE		1	69.549	55.462	0.345	1.00 67.48	
	MOTA	6565		PHE		1	67.410	55.116	-1.409	1.00 68.65	
50	MOTA	6566		PHE		1	69.548	54.364	-0.528	1.00 67.48	
	ATOM	6567	CZ	PHE		1	68.481	54.185	-1.406	1.00 69.10	
	ATOM	6568	С	PHE	E	1	67.191	59.419	2.218	1.00 61.93	
	MOTA	6569	Ō	PHE		1	67.898	59.384	3.225	1.00 62.32	
	MOTA	6570	N	PHE		1	68.457	59.591	0.037	1.00 62.93	
55	MOTA	6571	CA	PHE	$\mathbf{E}$	1	67.655	58.712	0.943	1.00 62.89	9 6
	MOTA	6572	N	ASP		2	66.011	60.038	2.205	1.00 61.01	
	MOTA	6573	CA	ASP		2	65.524	60.730	3.406	1.00 60.82	
	MOTA	6574	CB	ASP		2	64.448	61.754	3.027	1.00 59.66	
00	ATOM	6575	CG	ASP		2	63.263	61.126	2.346	1.00 61.52	
60	MOTA	6576		ASP		2	62.587	60.347	3.035	1.00 62.72	
	MOTA	6577	OD2	ASP	E	2	63.006	61.396	1.142	1.00 60.96	5 8

	WO 01/58	8951								PCT/	<b>EP</b> 01/01	457
							-180					
	ATOM	6578	С	ASP	E	2	65.012	59.731	4.459	1.00	60.89	6
	ATOM	6579	Ō	ASP		2	64.990	58.525	4.216	1.00	62.95	8
	ATOM	6580	N	ARG		3	64.624	60.214	5.635	1.00	60.20	7
	ATOM	6581	CA	ARG	E	3	64.161	59.321	6.697	1.00		6
5	MOTA	6582	CB	ARG	E	3	63.746	60.128	7.933	1.00		. 6
	MOTA	6583	CG	ARG		3	64.906.	60.475	8.878	1.00		· 6
	MOTA	6584	CD	ARG		3	65.314	59.266	9.702	1.00		6
	ATOM	6585	NE	ARG		3	66.519	59.426	10.524	1.00		7 6
10	MOTA	6586	CZ	ARG		3	66.825	60.497 61.559	11.258 11.294	1.00 1.00		7
10	MOTA	6587 6588	NH1	ARG ARG		3 3	66.024 67.943	60.499	11.294	1.00		7
	ATOM ATOM	6589	NH2	ARG		3	63.008	58.447	6.244	1.00		6
	MOTA	6590	0	ARG		3	62.949	57.256	6.567	1.00		8
	MOTA	6591	N	ALA		4	62.102	59.033	5.473	1.00		7
15	MOTA	6592	CA	ALA		4	60.937	58.311	4.993	1.00		6
. •	ATOM	6593	CB	ALA		4	60.002	59.262	4.270	1.00	50.53	6
	ATOM	6594	C	ALA		4	61.342	57.168	4.075	1.00	53.00	6
	ATOM	6595	0	ALA	E	4	60.858	56.056	4.225	1.00	53.30	8
	MOTA	6596	N	ASP	E	5	62.235	57.443	3.132	1.00	54.00	7
20	ATOM	6597	CA	ASP	E	5	62.692	56.433	2.190		54.02	6
	MOTA	6598	CB	ASP		5	63.702	57.021	1.197	1.00		6
	MOTA	6599	CG	ASP		5	63.153	58.223	0.435	1.00		6
	MOTA	6600		ASP		5	62.018	58.154	-0.072	1.00		8
<b>^</b> -	MOTA	6601		ASP		5	63.864	59.247	0.327	1.00		8
25	ATOM	6602	C	ASP		5	63.341	55.278	2.924		54.45	6
	ATOM	6603	0	ASP		5	63.192	54.127	2.532		54.26 54.54	8 7
	MOTA	6604	N	ILE		6 6	64.060	55.582 54.535	3.997 4.755		55.28	6
	MOTA MOTA	6605 6606	CA CB	ILE		6	64.734 65.727	55.121	5.781		56.90	6
30	MOTA	6607	CG2			6	66.476	53.991	6.489		56.40	6
00	ATOM	6608	CG1			6	66.728	56.031	5.068		58.74	6
	ATOM	6609		ILE		6	67.833	56.589	5.976		60.73	6
	ATOM	6610	C	ILE		6	63.765	53.617	5.482	1.00	53.47	6
	ATOM	6611	0	ILE	E	6	63.830	52.401	5.322	1.00	53.23	8
35	ATOM	6612	N	LEU	E	7	62.883	54.199	6.290		53.23	7
	MOTA	6613	CA	LEU	E	7	61.897	53.423	7.033		52.57	6
	MOTA	6614	CB	LEU		7	61.060	54.354	7.899		52.03	6
	MOTA	6615	CG	LEU	E	7	61.862	55.020	9.017		52.39	6
40	ATOM	6616		LEU		7	61.074	56.183	9.607		53.72	6
40	ATOM	6617		LEU		7	62.185	53.989	10.070		47.50	6
	ATOM	6618	C	LEU		7	61.003	52.660	6.065		52.40 53.43	6 8
	MOTA	6619	0	LEU		7	60.665 60.644	51.503 53.311	6.302 4.967		51.20	7
	ATOM	6620	N	TYR TYR		8 8	59.810	52.707	3.951		52.74	6
45	ATOM ATOM	6621 6622	CA CB	TYR		8	59.622	53.686	2.804		54.75	6
40	ATOM	6623	CG	TYR		8	58.825	53.102	1.660		60.00	6
	ATOM	6624	CD1			8	57.448	52.902	1.773		59.81	6
	ATOM	6625		TYR		8	56.723	52.341	0.734	1.00	59.72	6
	ATOM	6626		TYR		8	59.453	52.717	0.465	1.00	61.59	6
50	MOTA	6627	CE2			8	58.727	52.148	-0.580		59.67	6
	ATOM	6628	CZ	TYR	E	8	57.367	51.967	-0.433		59.94	6
	MOTA	6629	OH	TYR		8	56.646	51.411	-1.457		63.44	8
	MOTA	6630	. C	TYR		8	60.399	51.405	3.404		54.02	6
	ATOM	6631	0	TYR		8	59.692	50.414	3.259		54.84	8
55	ATOM	6632	N	ASN		9	61.688	51.411	3.082		53.58	7
	ATOM	6633	CA	ASN		9	62.338	50.224	2.559		52.96 58.69	6
	MOTA	6634	CB	ASN		9	63.790 63.907	50.524 51.445	2.182 0.966		62.10	6 6
	ATOM	6635	CG OD1	ASN ASN		9 9	63.907 62.908	51.445	0.321		64.59	8
60	MOTA MOTA	6636 6637		ASN		9	65.137	51.861	0.645		63.43	7
50	ATOM	6638	C	ASN		9	62.297	49.112	3.584		52.17	6
			_			_						

	WO 01/58	8951							PCT/EP01/014	157
						-181				
	MOTA	6639	0	ASN E	<b>5</b> 9	61.870	48.003	3.287	1.00 51.04	8
	ATOM	6640	N	ILE E		62.746	49.410	4.794	1.00 53.05	7
	ATOM	6641	CA	ILE E		62.752	48.424	5.866	1.00 53.91	6
_	MOTA	6642	CB	ILE E		63.189	49.053	7.195	1.00 53.67	6
5	ATOM	6643	CG2	ILE E		63.060	48.027	8.316	1.00 51.86 1.00 51.89	. 6 . 6
	MOTA	6644	CG1	ILE E		64.627	49.564	7.077	1.00 51.09	6
	MOTA	6645	CD1	ILE E		65.085 61.358	50.379 47.835	8.251 6.054	1.00 55.10	6
	MOTA	6646 6647	C	ILE E		61.186	46.631	6.216	1.00 55.00	8
10	MOTA MOTA	6648	N O	ARG I		60.364	48.708	6.032	1.00 56.28	7
	ATOM	6649	CA	ARG I		58.975	48.308	6.199	1.00 57.92	6
	ATOM	6650	CB	ARG I		58.084	49.543	6.106	1.00 61.96	6
	ATOM	6651	CG	ARG F	E 11	56.628	49.280	6.323	1.00 69.38	6
	ATOM	6652	CD	ARG I	E 11	56.359	49.040	7.797	1.00 79.46	6
15	MOTA	6653	NE	ARG I		54.957	49.274	8.149	1.00 85.84	7
	MOTA	6654	CZ	ARG I		54.244	50.315	7.713	1.00 89.11 1.00 90.35	6 7
	MOTA	6655	NH1	ARG I		54.801	51.215	6.892 8.117	1.00 90.33	7
•	MOTA	6656	NH2	ARG I		52.980 58.559	50.475 47.314	5.126	1.00 56.77	6
20	ATOM ATOM	6657 6658	C 0	ARG I		57.986	46.264	5.415	1.00 55.32	8
20	MOTA	6659	<b>M</b>	GLN I		58.866	47.663	3.881	1.00 56.51	7
	MOTA	6660	CA	GLN I		58.511	46.850	2.730	1.00 54.24	6
	ATOM	6661	CB	GLN I		58.583	47.698	1.485	1.00 53.75	6
	MOTA	6662	CG	GLN I	E 12	57.341	47.645	0.673	1.00 58.35	6
25	MOTA	6663	CD	GLN 1		56.287	48.540	1.223	1.00 59.21	6
	MOTA	6664	OE1	GLN !		56.517	49.726	1.375	1.00 63.59	8
	MOTA	6665		GLN :		55.121	47.990	1.528	1.00 59.83 1.00 53.65	7 6
	ATOM	6666	C	GLN :		59.312	45.581 44.677	2.484 1.825	1.00 52.67	8
30	MOTA	6667	0	GLN :		58.820 60.536	45.507	2.995	1.00 54.14	7
30	MOTA MOTA	6668 6669	N CA	THR		61.369	44.331	2.771	1.00 55.96	6
	ATOM	6670	CB	THR		62.714	44.726	2.181	1.00 55.93	6
	ATOM	6671	OG1	THR		63.380	45.612	3.090	1.00 55.29	8
	ATOM	6672		THR		62.526	45.400	0.822	1.00 55.33	6
35	ATOM	6673	С	THR		61.656	43.486	4.005	1.00 58.24	б
	MOTA	6674	0	THR		62.096	42.343	3.892	1.00 58.85	8
	MOTA	6675	N	SER		61.414	44.042	5.182	1.00 60.49	7
	ATOM	6676	CA	SER		61.681	43.317	6.408	1.00 61.17 1.00 62.69	6 6
40	MOTA	6677	CB	SER		61.629 62.247	44.265 43.658	7.599 8.723	1.00 62.89	8
40	ATOM	6678	OG	SER			43.050	6.644	1.00 60.16	6
	ATOM ATOM	6679 6680	C 0	SER SER			42.153	6.184	1.00 59.94	8
	ATOM	6681	N	ARG			41.156	7.369	1.00 58.70	7
	ATOM	6682	CA	ARG			39.949	7.703	1.00 58.01	6
45	MOTA	6683	CB	ARG			38.792	6.805	1.00 57.94	6
	ATOM	6684	CG	ARG	E 15	60.686	39.058	5.325	1.00 59.93	6
	MOTA	6685	CD	ARG			37.761	4.547	1.00 63.77	6
	ATOM	6686	NE	ARG			36.818	5.060	1.00 66.81	7
	ATOM	6687	CZ	ARG			35,516	4.772	1.00 66.79 1.00 64.79	6 7
50	ATOM	6688		ARG			34.982 34.752	3.964 5.287	1.00 67.36	. 7
	ATOM ATOM	6689	C NHZ	ARG ARG			39.621	9.170	1.00 55.75	6
	ATOM	6690 6691	0	ARG			38.928	9.513	1.00 55.70	8
	ATOM	6692	N	PRO			40.121	10.057	1.00 54.09	7
55	ATOM	6693	CD	PRO			40.932	9.727	1.00 50.97	6
	MOTA	6694	CA	PRO	E 16		39.919	11.503	1.00 51.94	6
	MOTA	6695	CB	PRO			40.650	12.031	1.00 50.89	6
	MOTA	6696	CG	PRO			41.680	10.997	1.00 51.98	6
00	ATOM	6697	C	PRO			38.473	11.945	1.00 50.22 1.00 49.19	6 8
60	MOTA	6698	0	PRO			38.176 37.579	13.046 11.095	1.00 49.19	7
	MOTA	6699	N	ASP	- I	33.312	31.313	11.000	2.00 00.70	'

	WO 01/5	8951								PCT/EP01/01	457
	:						-182				
	ATOM	6700	CA	ASP 1	FC 1	L7	59. <b>4</b> 77	36.171	11.446	1.00 53.11	6
	ATOM	6701		ASP 1		.7	58.244	35.492	10.832	1.00 58.78	6
	ATOM	6702		ASP 1		17	56.931	35.917	11.513	1.00 64.95	6
	ATOM	6703	-	ASP		L7	56.959	36.261	12.732	1.00 65.29	8 .
5	ATOM	6704		ASP		17	55.865	35.887	10.831	1.00 66.80	8
-	ATOM	6705		ASP :		L7.	60.716	35.401	11.039	1.00 52.04	6
	ATOM	6706	0	ASP :	E :	L7	60.787	34.194	11.242	1.00 53.16	8
	ATOM	6707	N	VAL	E :	18	61.701	36.090	10.481	1.00 52.13	7
	MOTA	6708		VAL		18	62.906	35.410	10.034	1.00 51.75	6
10	ATOM	6709	_	VAL		18	63.050	35.519	8.509	1.00 53.20	6
	ATOM	6710		VAL		18	64.265	34.728	8.037	1.00 54.22	6 6
	MOTA	6711	-	VAL		18	61.797	35.010	7.843	1.00 52.93 1.00 50.84	6
	ATOM	6712	C	VAL		18	64.193	35.897	10.675 10.513	1.00 50.84	8
1 =	ATOM	6713	0	VAL		18 19	64.595 64.841	37.039 34.990	11.387	1.00 50.74	7
15	MOTA	6714 6715	N	ILE. ILE		19 19	66.092	35.270	12.077	1.00 53.80	6
	ATOM ATOM	6715 6716	CA CB	ILE		19	66.478	34.027	12.940	1.00 52.99	6
	ATOM	6717	CG2	ILE		19	66.791	32.842	12.040	1.00 52.72	6
	ATOM	6718		ILE		19	67.644	34.346	13.870	1.00 52.81	6
20	ATOM	6719	CD1	ILE		19	67.867	33.290	14.923	1.00 49.41	6
	ATOM	6720	С	ILE	E	19	67.184	35.628	11.053	1.00 55.50	6
	MOTA	6721	0	ILE	E	19	67.399	34.903	10.087	1.00 54.87	8
	MOTA	6722	N	PRO		20	67.879	36.765	11.250	1.00 57.80	7
	ATOM	6723	CD	PRO		20	67.710	37.684	12.385	1.00 58.20	6
25	MOTA	6724	CA	PRO		20	68.948	37.253	10.359	1.00 60.68	6
	MOTA	6725	CB	PRO		20	69.252	38.664	10.897	1.00 58.99 1.00 60.19	6 6
	ATOM	6726	CG	PRO		20	68.056 70.201	39.007 36.370	11.744 10.360	1.00 60.19	6
	MOTA	6727 6728	C O	PRO PRO		20 20	71.317	36.854	10.568	1.00 61.22	8
30	ATOM ATOM	6728	N	THR		21	70.008	35.080	10.117	1.00 65.32	7
00	ATOM	6730	CA	THR		21	71.107	34.128	10.106	1.00 69.19	6
	ATOM	6731	CB	THR		21	70.573	32.698	10.364	1.00 68.56	6
	ATOM	6732	OG1	THR	E	21	70.744	32.370	11.751	1.00 66.59	8
_	ATOM	6733	CG2	THR		21	71.300	31.677	9.502	1.00 68.21	6
35	MOTA	6734	С	THR		21	71.964	34.121	8.840	1.00 72.78	6
	MOTA	6735	0	THR		21	71.450	34.096	7.716	1.00 72.75 1.00 77.19	8 7
	ATOM	6736	N	GLN		22	73.282	34.128 34.102	9.051 7.971	1.00 77.19	6
	MOTA	6737	CA	GLN GLN		22 22	74.279 75.303	35.209	8.192	1.00 81.20	6
40	MOTA	6738 6739	CB CG	GLN		22	74.691	36.597	8.264	1.00 83.07	6
40	MOTA MOTA	6740	CD	GLN		22	75.515	37.542	9.131	1.00 85.11	6
	ATOM	6741	OE1			22	75.640	37.329	10.355	1.00.85.67	8
	ATOM	6742	NE2			22	76.087	38.587	8.510	1.00 84.48	7
	ATOM	6743	C	GLN		22	74.980	32.739	8.023	1.00 81.85	, 6
45	MOTA	6744	0	GLN	E	22	75.783	32.480	8.929	1.00 81.74	8
	MOTA	6745	N	ARG		23	74.676	31.880	7.050	1.00 84.04	7
	MOTA	6746		ARG		23	75.235	30.521	7.001	1.00 84.92	6
	ATOM	6747	CB	ARG		23	76.767	30.550	6.931	1.00 84.82 1.00 87.29	6 6
<b>5</b> 0	ATOM	6748	CG	ARG		23	77.314 77.788	30.929 32.397	5.558 5.462	1.00 87.23	6
50	MOTA	6749 6750	CD NE	ARG ARG		23 23	78.140	32.777	4.081	1.00 92.74	7
	MOTA MOTA	6751	CZ	ARG		23	78.982	32.103	3.287	1,00 93.28	6
	ATOM	6752		ARG		23	79.592	30.993	3.712	1.00 92.22	7
	ATOM	6753		ARG		23	79.204	32.535	2.047	1.00 92.78	7
55	MOTA	6754	C	ARG		23	74.790	29.736	8.237	1.00 85.32	6
	MOTA	6755	0	ARG		23	73.673	29.929	8.747	1.00 85.55	8
	MOTA	6756	N	ASP		24	75.648	28.842	8.718	1.00 85.95	7
	ATOM	6757	CA	ASP		24	75.304	28.062	9.907	1.00 86.37 1.00 90.45	6 6
60	MOTA	6758	CB	ASP ASP		24 24	76.103 76.671	26.752 26.317	9.985 8.636	1.00 90.45	6
50	MOTA MOTA	6759 6760	CG OD1	ASP ASP		24	75.856	26.082	7.698	1.00 95.19	8
	011	5,50			_				-		

	WO 01/58	8951							PCT/EP01/014	157
						-183				_
	MOTA	6761	OD2	ASP E	24	77.930	26.212	8.533	1.00 94.96	8
	ATOM	6762	С	ASP E	24	75.657	28.917	11.116	1.00 84.76	6
	ATOM	6763	0	ASP E	24	75.551	28.466	12.259	1.00 84.92	8
	ATOM	6764	N	ARG E	25	76.097	30.146	10.857	1.00 82.51	7
5	ATOM	6765	CA	ARG E	25	76.465	31.063	11.930	1.00 80.45	6
	MOTA	6766	CB	ARG E	25	77.208	32.289	11.382	1.00 83.04	6
	ATOM	6767	CG	ARG E	25	78.635	32.032	10.918	1.00 87.73	6
	MOTA	6768	CD	ARG E	25	79.370	33,358	10.688	1.00 91.97	6 7
	MOTA	6769	NE	ARG E	25	80.781	33.171	10.340	1.00 95.94	6
10	MOTA	6770	CZ	ARG E	25	81.667	34.164	10.199	1.00 97.73 1.00 98.12	7
	MOTA	6771	NH1	ARG E	25	81.285	35.435	10.379	1.00 98.12	7
	MOTA	6772	NH2	ARG E	25	82.938	33.892	9.880	1.00 97.12	6
	ATOM	6773	С	ARG E	25	75.256	31.557	12.708	1.00 76.34	8
	ATOM	6774	0	ARG E	25	74.265	31.999	12.122	1.00 73.86	7
15	MOTA	6775	N	PRO E	26	75.322	31.483	14.045	1.00 73.05	6
	MOTA	6776	CD	PRO E	26	76.343	30.778	14.834	1.00 70.73	6
	ATOM	6777	CA	PRO E	26	74.231	31.936	14.916 16.295	1.00 70.73	6
	MOTA	6778	CB	PRO E	26	74.647	31.425	15.984	1.00 70.33	6
	ATOM	6779	CG	PRO E	26	75.529	30.257	14.891	1.00 67.63	6
20	ATOM	6780	С	PRO E	26	74.199	33.466 34.110	14.691	1.00 66.91	8
	ATOM	6781	0	PRO E	26	75.173	34.110	15.288	1.00 63.36	7
	MOTA	6782	N	VAL E	27	73.076 72.980	35.487	15.346	1.00 57.94	6
	MOTA	6783	CA	VAL E	27	72.560	35.949	15.266	1.00 55.79	6
0-	MOTA	6784	CB	VAL E	27	71.403	37,366	15.780	1.00 54.61	6
25	MOTA	6785		VAL E	27 27	71.082	35.870	13.839	1.00 57.04	6
	MOTA	6786		VAL E		73.554	35.821	16.706	1.00 57.83	6
	ATOM	6787	C	VAL E	27 27	73.334	35.207	17.711	1.00 58.05	8
	ATOM	6788	0	VAL E	28	74.490	36.760	16.744	1.00 55.79	7
20	MOTA	6789	N	ALA E	28	75.087	37,130	18.014	1.00 55.59	6
30	MOTA	6790	CA CB	ALA E	28	76.508	37.588	17.810	1.00 54.25	6
	MOTA	6791 6792	C	ALA E		74.270	38.224	18.677	1.00 54.76	6
	MOTA MOTA	6793	o	ALA E		74.244	39.370	18.216	1.00 54.28	8
		6794	N	VAL E		73.596	37.850	19.759	1.00 53.10	7
35	ATOM ATOM	6795	CA	VAL E		72.769	38.783	20.514	1.00 53.62	6
33	MOTA	6796	CB	VAL E		71.338	38.222	20.767	1.00 52.63	6
	MOTA	6797		L VAL E		70.531	39.210	21.591	1.00 47.51 [.]	6
	ATOM	6798		VAL E		70.641	37.940	19.446	1.00 52.51	6
	MOTA	6799		VAL E		73.412	39.051	21.865	1.00 53.21	6
40	MOTA	6800		VAL E		73.760		22.599	1.00 53.58	8
10	MOTA	6801	-	SER E		73.583	40.325	22.184	1.00 51.51	7
	ATOM	6802		SER E		74.154	40.681	23.459	1.00 54.05	٠6
	ATOM	6803		SER E	30	75.288	41.690	23.276	1.00 52.43	6
	ATOM	6804		SER E	30	74.821		22,632	1.00 55.74	8
45	ATOM	6805		SER E		73.024		24.301		6
	MOTA	6806		SER E	30	72.236		23.825		8
	MOTA	6807		VAL E	31	72.946				7
	MOTA	6808		VAL I	31	71.934				6
	MOTA	6809	СВ	VAL I	31	71.058				6
50	MOTA	6810		1 VAL I	31	69.842	_			6
	MOTA	6811	. CG	2 VAL I	₃ 31	70.653				6
	MOTA	6812		VAL I		72.599				6
	MOTA	6813	3 0	VAL 1		73.542		_		8
	MOTA	6814	1 N	SER I		72.092				7
55	MOTA	6815				72.648				6 6
	MOTA	6816	5 CB			73.688				6 8
	MOTA	6817	7 OG			74.162				6
	MOTA	6818		SER		71.552				8
	MOTA			SER		70.943				7
60				LEU		71.300				6
	MOTA	. 682	1 CA	LEU	E 33	70.282	. <del></del>	. 55,10.		-

	WO 01/5	8951								PCT	/EP01/01	457
							-184					
	MOTA	6822	CB	LEU I	E	33	69.658	3 43.578	33.122	1.00 5	54.43	6
	ATOM	6823	CG	LEU :		33	69.031		32.487	1.00	55.79	6
	ATOM	6824		LEU	E	33	68.247	7 41.561	33.532	1.00	_	6
	ATOM	6825		LEU		33	68.132	2 42.781	31.348	1.00 !		6
5	ATOM	6826	С	LEU	E	33	70.880		32.985	1.00		6
	MOTA	6827	0	LEU	Ε	33	71.95		33.556	1.00		8
	MOTA	6828	N	LYS		34	70.18		33.029	1.00		7
	MOTA	6829	CA	LYS		34	70.61		33.822	1.00		6
40	MOTA	6830	CB	LYS		34	70.799		32.948	1.00		6
10	MOTA	6831	CG	LYS		34	71.72		31.774	1.00		6 6
	ATOM	6832	CD	LYS		34	73.179 74.10		32.205 30.973	1.00		6
	ATOM	6833	CE	LYS		34 34	75.54		31.351	1.00		7
	MOTA MOTA	6834 6835	NZ C	LYS LYS		34	69.45		34.776	1.00		6
15	ATOM	6836	0	LYS		34	68.37		34.356	1.00		8
10	ATOM	6837	N	PHE		35	69.66		36.059	1.00		7
	MOTA	6838	CA	PHE		35	68.58		37.011	1.00	49.05	6
	MOTA	6839	CB	PHE		35	68.89		38.292	1.00	46.62	6
•	MOTA	6840	CG	PHE		35	68.92	1 45.883	38.095	1.00		6
20	ATOM	6841		PHE	E	35	70.07	1 45.254	37.651	1.00	46.38	6
	ATOM	6842		PHE		35	67.76	6 45.125	38.253	1.00		6
	MOTA	6843	CE1	PHE	Ε	35	70.07		37.363	1.00		6
	MOTA	6844	CE2	PHE	E	35	67.75		37.964	1.00		6
	MOTA	6845	CZ	PHE	Ε	35	68.91		37.517		48.13	6
25	MOTA	6846	С	PHE		35	68.22		37.285		48.83	6
	MOTA	6847	0	PHE		35	69.08		37.492		50.99	8
	MOTA	6848	N	ILE		36	66.92		37.259		47.58	7 6
	ATOM	6849	CA	ILE		36	66.40		37.465		44.93 44.37	6
00	ATOM	6850	CB	ILE		36	65.39		36.370 36.547		39.93	6
30	MOTA	6851	CG2			36	64.92 66.03		34.994		45.24	6
	MOTA	6852		ILE ILE		36 36	67.29		34.776		46.74	6
	ATOM ATOM	6853 6854	CDI	ILE		36	65.69		38.792		46.03	6
	ATOM	6855	0	ILE		36	65.58		39.347		46.58	8
35	MOTA	6856	N	ASN		37	65.20		39.299		45.38	7
00	MOTA	6857	CA	ASN		37	64.51		40.580	1.00	44.10	6
	MOTA	6858	CB	ASN		37	63.25		40.471	1.00	42.99	6
	ATOM	6859	CG	ASN		37	62.87	0 51.660	41.784	1.00	46.14	6
•	MOTA	6860	OD1	ASN	E	37	62.89		42.832		45.55	.8
40	MOTA	6861	ND2	ASN	E	37	62.49	7 52.931	41.731		45.29	7
	MOTA	6862	С	ASN	E	37	64.12				45.25	6
	MOTA	6863	0	ASN		37	64.00		40.317		42.90	8
	MOTA	6864	N	ILE		38	63.95		42.401		46.26	7
40	MOTA	6865	CA	ILE		38	63.53		43.057		47.22	6
45	MOTA	6866	CB	ILE		38	64.64		43.940 44.685		46.57 46.43	6 6
	MOTA	6867		ILE		38 38	64.15 65.84		43.058		47.22	6
•	MOTA MOTA	6868 6869		ILE ILE		38	67.10		43.784		46.51	6
	MOTA	6870	C	ILE		38	62.34		43.879		48.14	6
50	MOTA	6871	Ö	ILE		38	62.50		44.855		49.04	8
-	ATOM	6872	N	LEU		39	61.15		43.466	1.00	49.65	7
	ATOM	6873	CA	LEU		39	59.90		44.092	1.00	51.44	6
	MOTA	6874	CB	LEU		39	58.85		43.004		53.02	6
	MOTA	6875	CG	LEU		39	59.35				54.99	6
55	ATOM	6876		LEU	E	39	58.31				54.07	6
	MOTA	6877		LEU		39	59.71				53.65	6
	MOTA	6878		LEU		39	59.33				52.90	6
	MOTA	6879		LEU		39	58.79				53.53	8
	MOTA	6880		GLU		40	59.33				54.20	7
60	ATOM	6881		GLU		40	58.78				56.14	6
	MOTA	6882	CB	GLU	E	40	57.3	57 44.549	45.960	1.00	58.59	6

	WO 01/58	8951								PCT	/ <b>EP01</b> /01	1457
							-185					
	MOTA	6883	CG	GLU	E	40	56.377	45.678	45.865	1.00		6
	MOTA	6884	CD	GLU :	E	40	54.960	45.178	45.718	1.00		6
	ATOM	6885	OE1	GLU :	E	40	54.697	44.405	44.757	1.00		8
	MOTA	6886	OE2	GLU	E	40	54.119	45.561	46.564		69.89	8
5	MOTA	6887	С	GLU .	E	40	59.620	43.773	46.449		55.88	6
	MOTA	6888	0	GLU	E	40	60.029	43.134	45.498		58.42	8
	MOTA	6889	N	VAL		41	59.876	43.454	47.700		55.75	7
	MOTA	6890	CA	VAL		41	60.675	42.300	48.021		55.46	6
	MOTA	6891	CB	VAL		41	62.067	42.732	48.550		56.94	6
10	MOTA	6892		VAL		41	62.802	41.547	49.107		58.11	6
	MOTA	6893		VAL		41	62.878	43.361	47.433		55.88	6
	MOTA	6894	С	VAL		41	59.925	41.520	49.078		55.20	6
	MOTA	6895	0	VAL		41	59.230	42.094	49.908		55.44	8
4 =	ATOM	6896	N	ASN		42	60.042	40.204	49.025		55.58 56.97	7 6
15	ATOM	6897	CA	ASN		42	59.381	39.350	49.995		55.95	6
	ATOM	6898	CB	ASN		42	58.077	38.794	49.430 50.490		55.31	6
	MOTA	6899	CG OD1	ASN ASN		42 42	57.220 57.696	38.135 37.306	51.267		56.29	8
	MOTA	6900 6901		ASN		42	55.948	38.499	50.526		53.42	7
20	ATOM ATOM	6902	C ND2	ASN		42	60.360	38.222	50.320		59.68	6
20	ATOM	6903	0	ASN		42	60.527	37.337	49.393		60.84	8
	ATOM	6904	N	GLU		43	61.014	38.255	51.398		61.29	7
	ATOM	6905	CA	GLU		43	62.005	37.242	51.717		62.43	6
	MOTA	6906	CB	GLU		43	62.898	37.721	52.857		65.13	6
25	ATOM	6907	CG	GLU		43	64.066	36.787	53.120		70.44	6
	ATOM	6908	CD	GLU		43	65.091	37.358	54.094		73.76	6
	ATOM	6909		GLU		43	66.010	36.601	54.486	1.00	74.81	8
	ATOM	6910	OE2			43	64.982	38.557	54.460	1.00	74.43	8
	MOTA	6911	С	GLU	E	43	61.355	35.920	52.070		61.19	6
30	ATOM	6912	0	GLU	E	43	61.977	34.861	51.958		58.53	8
	ATOM	6913	N	ILE	E	44	60.094	35.994	52.484		61.32	7
	ATOM	6914	CA	ILE		44	59.330	34.809	52.852		61.37	6
	MOTA	6915	CB	ILE	Ε	44	57.999	35.178	53.536		62.70	6
	MOTA	6916	CG2	ILE		44	57.197	33.897	53.812		63.01	6
35	ATOM	6917	CG1			44	58.258	35.946	54.836		62.78	6
	MOTA	6918		ILE		44	58.852	35.088	55.947		63.28	6
	ATOM	6919	С	ILE		44	58.983	34.000	51.608		60.40	6
	ATOM	6920	0	ILE		44	59.114	32.774	51.592		61.80	8 7
40	ATOM	6921	N	THR		45	58.532	34.692	50.569		58.56 57,28	6
40	ATOM	6922	CA	THR		45	58.149	34.033	49.326			_
	ATOM	6923	CB	THR		45	56.906 57.100	34.696 36.074	48.710 48.443		56.47 55.94	6 8
	MOTA	6924		THR		45. 45	57.189 55.724	34.588	49.658		52.56	6
	MOTA	6925	CGZ	THR		45	59.245	34.029	48.275		55.65	6
45	ATOM	6926 6927	0	THR		45	59.120	33.357	47.262		55.71	8
40	ATOM ATOM	6928	N	ASN		46	60.313	34.782	48.514		55.17	7
	ATOM	6929	CA	ASN		46	61.420	34.850	47.564		54.46	6
	ATOM	6930	CB	ASN		46	62.057	33.472	47.435		54.61	6
	ATOM	6931	CG	ASN		46	63.288	33.322	48.290		56.45	6
50	ATOM	6932		ASN		46	63.674	32.213	48.638		57.64	8
•	ATOM	6933		ASN		46	63.922	34.436	48.621	1.00	53.06	7
	ATOM	6934	C	ASN		46	60.972	35.362	46.187	1.00	54.17	6
	ATOM	6935	ŏ	ASN		46	61.259	34.764	45.149	1.00	54.29	8
	ATOM	6936	N	GLU		47	60.267	36.482	46.191		52.96	7
55	ATOM	6937	CA	GLU		47	59.769	37.074	44.970		·51.83	6
	ATOM	6938	CB	GLU	E	47	58.247	36.956	44.926		50.20	6
	ATOM	6939	CG	GLU	E	47	57.750		44.856		50.29	6
	MOTA	6940	CD	GLU		47	56.236		44.877		52.98	6
_	ATOM	6941	OE1			47	55.589	36.442	44.516		50.88	8
60	MOTA	6942		GLU		47	55.692		45.237		56.10	8
	ATOM	6943	С	GLU	E	47	60.186	38.534	44.919	Τ.00	51.43	6

	WO 01/5	8951								PCT/EP01/01	457
							-186				
	ATOM	6944	0	GLU E	47		60.134	39.243	45.919	1.00 51.14	8
	MOTA	6945	N	VAL E	48		60.597	38.980	43.742	1.00 51.27	7
	ATOM	6946	CA	VAL E	48		61.037	40.352	43.574	1.00 51.20	6
	ATOM	6947	CB	VAL E	48		62.554	40.402	43.276	1.00 52.39	6
5	ATOM	6948	CG1	VAL E	48		63.000	41.822	43.081	1.00 54.32	6
	MOTA	6949	CG2	VAL E	48		63.319	39.778	44.411	1.00 53.03	6
	ATOM	6950	С	VAL E	48		60.290	41.062	42.452	1.00 49.53	6
	ATOM	6951	0	VAL E	48		59.974	40.474	41.425	1.00 47.97	8
	MOTA	6952	N	ASP E			60.005	42.334	42.669	1.00 47.94	7
10	MOTA	6953	CA	ASP E			59.335	43.146	41.680	1.00 48.29	6
	MOTA	6954	CB	ASP E			58.107	43.795	42.290	1.00 49.64	6
	MOTA	6955	CG	ASP E			57.146	44.300	41.249	1.00 50.04 1.00 47.78	6 8
	MOTA	6956		ASP E			57.596	44.853	40.228 41.459	1.00 47.78	8
4 =	ATOM	6957		ASP E			55.931	44.151 44.200 ·		1.00 33.33	6
15	ATOM	6958	C	ASP E			60.373 60.644	45.101	42.118	1.00 48.55	8
	ATOM	6959	0	ASP E			60.950	44.085	40.140	1.00 48.88	7
	ATOM	6960 6961	N CA	VAL E			62.011	44.988	39.718	1.00 48.55	6
	MOTA MOTA	6962	CB	VAL E			63.353	44.220	39.707	1.00 50.40	6
20	MOTA	6963		VAL E			63.428	43.303	38.492	1.00 49.66	6
20	ATOM	6964		VAL E			64.511	45.188	39.721	1.00 55.70	6
	MOTA	6965	C	VAL E			61.801	45.642	38.354	1.00 47.28	6
	ATOM	6966	ō	VAL E			61.057	45.134	37.523	1.00 48.34	8
	MOTA	6967	N	VAL E			62.467	46.777	38.144	1.00 45.37	7
25	ATOM	6968	CA	VAL E	51		62.407	47.540	36.896	1.00 43.25	6
	ATOM	6969	CB	VAL E	51		61.930	48.993	37.131	1.00 41.43	6
	ATOM	6970	CG1	VAL E			62.118	49.820	35.865	1.00 39.28	6
	ATOM	6971	CG2	VAL E			60.478	49.000	37.546	1.00 39.33	6
	ATOM	6972	С	VAL I			63.821	47.597	36.333	1.00 44.33	6
30	MOTA	6973	0	VAL I			64.764	47.841	37.078	1.00 46.78	8
	MOTA	6974	N	PHE I			63.978	47.383	35.029	1.00 43.60	7 6
	MOTA	6975	CA	PHE I			65.304	47.416 46.085	34.430 34.678	1.00 41.93 1.00 41.48	6
•	MOTA	6976	CB	PHE I		٠	65.997 65.275	44.917	34.070	1.00 41.48	6
35	MOTA	6977 6978	CG	PHE I			65.486	44.566	32.745	1.00 42.10	6
30	ATOM ATOM	6979		PHE I			64.347	44.200	34.809	1.00 43.51	6
	ATOM	6980		PHE I			64.784	43.527	32.167	1.00 42.36	6
	MOTA	6981	CE2				63.638	43.153	34.236	1.00 45.87	6
	MOTA	6982	CZ	PHE !			63.859	42.818	32.911	1.00 43.76	6
40	ATOM	6983	C	PHE 1			65.239	47.675	32.933	1.00 44.18	6
, -	MOTA	6984	Ō	PHE 1			64.183	47.574	32.314	1.00 43.22	8
	ATOM	6985	N	TRP 1	E 53		66.384	48.014	32.354	1.00 46.10	7
	ATOM	6986	CA	TRP 1			66.466	48.252	30.927	1.00 47.08	6
	ATOM	6987	CB	TRP 1			67.367	49.431	30.614	1.00 46.54	6
45	ATOM	6988	CG	TRP 1			66.822	50.726	31.015	1.00 49.25	6
	MOTA	6989		TRP :			67.510	51.972	30.991	1.00 51.55	6
	MOTA	6990		TRP			66.616	52.951	31.471	1.00 52.89	6
	MOTA.	6991		TRP			68.804	52.358	30.614	1.00 53.33 1.00 50.42	6 6
EΛ	MOTA	6992		TRP :			65.577 65.440	50.980 52.318	31.486 31.765	1.00 50.42	7
50	MOTA	6993		TRP			66.969	54.299	31.789	1.00 54.65	6
	MOTA	6994	CZ3				69.162	53.706	30.730	1.00 55.02	6
	MOTA MOTA	6995 6996		TRP			68.245	54.658	31.215	1.00 56.13	6
	MOTA	6997	Ch2	TRP			67.070	47.018	30.316	1.00 48.44	6
55	ATOM	6998	Ö	TRP			68.201	46.680	30.616	1.00 50.00	8
	ATOM	6999	N	GLN			66.313	46.342	29.465	1.00 49.02	7
	MOTA	7000	CA	GLN			66.805	45.143	28.818	1.00 49.56	6
	MOTA	7001	СВ	GLN			65.648	44.193	28.517	1.00 50.24	6
	MOTA	7002	CG	GLN			66.076	42.837	28.017	1.00 52.86	6
60	MOTA	7003	CD	GLN			65.043	41.768	28.313	1.00 57.64	6
	MOTA	7004	OE1	GLN	E 54		64.668	41.564	29.465	1.00 59.29	8

ATOM   7005   NE2   GLN E   54   64.576   61.078   27.275   1.00   58.15   7		WO 01/5	8951								PCT	/ <b>EP</b> 01/01	1457
ATOM 7006 C GINN E 54 67.500 45.583 27.547 1.00 50.68 6 ATOM 7007 O GINN E 54 66.972 45.458 26.446 1.00 50.318 6 ATOM 7008 N GINN E 55 68.692 46.132 27.735 1.00 53.08 7 ATOM 7008 N GINN E 55 68.692 46.132 27.735 1.00 53.08 7 ATOM 7010 CG GINN E 55 70.723 47.342 27.257 1.00 57.75 6 ATOM 7011 CG GINN E 55 70.723 47.342 27.257 1.00 57.75 6 ATOM 7012 CD GINN E 55 70.723 47.342 27.257 1.00 57.75 6 ATOM 7012 CD GINN E 55 70.723 47.342 26.952 1.00 70.80 6 ATOM 7012 CD GINN E 55 72.759 48.745 26.952 1.00 70.80 6 ATOM 7012 CD GINN E 55 73.254 49.710 26.175 1.00 70.30 7 ATOM 7014 NEZ GINN E 55 73.057 48.637 28.158 1.00 74.02 8 ATOM 7014 NEZ GINN E 55 73.057 48.637 28.158 1.00 74.02 8 ATOM 7015 CD GINN E 55 70.844 44.664 25.768 1.00 54.06 6 ATOM 7016 CD GINN E 55 70.844 44.664 25.768 1.00 54.06 6 ATOM 7017 N THR E 56 69.978 44.652 23.664 1.00 55.40 7 ATOM 7019 CB THR E 56 69.370 45.350 24.592 1.00 51.47 7 ATOM 7019 CB THR E 56 69.370 45.350 24.592 1.00 51.47 7 ATOM 7019 CB THR E 56 68.340 43.527 23.323 1.00 48.99 6 ATOM 7021 CG THR E 56 68.584 42.228 22.613 1.00 48.99 6 ATOM 7022 C THR E 56 68.584 42.228 22.613 1.00 48.99 6 ATOM 7021 CG THR E 56 69.978 44.780 22.374 1.00 48.56 6 ATOM 7022 C THR E 56 69.979 45.870 21.916 1.00 49.57 6 ATOM 7023 CD THR E 56 69.979 45.870 21.916 1.00 49.57 6 ATOM 7024 N THR E 57 71.778 44.370 20.545 1.00 48.63 6 ATOM 7025 CD THR E 57 71.778 44.370 20.545 1.00 48.63 6 ATOM 7026 CB THR E 57 72.766 46.569 1.00 47.16 8 ATOM 7027 CG THR E 57 72.766 46.569 1.504 1.00 47.16 8 ATOM 7031 N TRP E 58 69.919 45.870 20.545 1.00 48.03 6 ATOM 7032 C THR E 57 72.766 46.569 1.504 1.00 47.16 8 ATOM 7032 C THR E 57 72.766 46.369 1.504 1.00 47.16 8 ATOM 7033 CB THR E 57 72.766 46.369 1.504 1.00 47.16 8 ATOM 7035 CD THR E 58 69.489 1.489 1.9488 1.00 53.54 6 ATOM 7036 CD THR E 58 69.489 1.489 1.9488 1.00 53.54 6 ATOM 7037 CB THR E 58 69.489 1.189 1.189 1.00 44.125 6 ATOM 7036 CD THR E 58 69.489 1.189 1.189 1.00 44.125 6 ATOM 7037 CB THR E 58 69.489 1.189 1.189 1.00 44.125 6 ATOM 7036 CD THR E 58 69.489 1.189 1.189								-187					
ATOM   7006   C   GLN E   54   66.97.50   45.583   27.547   1.00   50.68   8   1.00   7007   7008   N   GLN E   54   66.972   45.458   26.446   1.00   50.31   8   1.00   7007   7009   CR   GLN E   55   68.592   46.622   26.647   1.00   57.75   6   68.700   7009   CR   ATOM   7010   CR   GLN E   55   70.723   47.342   27.257   1.00   57.75   6   6.700   7012   CD   GLN E   55   71.798   47.759   26.296   1.00   70.80   6   6   70.700   7012   CD   GLN E   55   71.798   47.759   26.296   1.00   70.80   6   6   70.700   7014   NE   GLN E   55   73.057   48.745   26.952   1.00   70.80   6   70.700   7014   NE   GLN E   55   73.057   48.637   28.188   1.00   74.02   8   70.700   7014   NE   GLN E   55   70.834   44.648   25.768   1.00   54.06   6   70.700   70.80   6   70.700   70.80   6   70.700   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80   70.80		ATOM	7005	NE2	GLN E	54		64.576	41.078	27.275			
ATOM   7009   N   GLN E   55   68.692   46.132   27.735   1.00   30.08   7		ATOM	7006	С	GLN F	54							
5 AROM 7009 CA GLNE 55 69.534 46.620 26.647 1.00 55.55 6 6 AROM 7011 CB GLN E 55 70.73 47.342 27.257 1.00 57.75 6 AROM 7011 CG GLN E 55 71.798 47.759 26.256 1.00 65.99 6 AROM 7013 OCI GLN E 55 71.798 47.759 26.266 1.00 65.99 6 AROM 7013 OCI GLN E 55 73.245 48.637 28.158 1.00 74.02 8 10 AROM 7014 NEZ GLN E 55 73.245 49.710 26.175 1.00 74.02 8 10 AROM 7015 C GLN E 55 73.245 49.710 26.175 1.00 74.02 8 10 AROM 7015 C GLN E 55 69.978 45.446 25.768 1.00 54.06 7 10 AROM 7017 N THR E 56 69.978 45.446 26.147 1.00 55.16 8 10 AROM 7017 N THR E 56 69.538 44.266 23.664 1.00 49.57 6 10 AROM 7019 CB THR E 56 69.538 44.266 23.664 1.00 49.57 6 10 AROM 7020 CG THR E 56 66.638 42.268 22.613 1.00 48.99 6 AROM 7021 CG2 THR E 56 66.638 42.268 22.613 1.00 48.99 6 AROM 7022 C THR E 56 69.919 45.870 22.374 1.00 48.95 6 AROM 7022 C THR E 57 71.131 43.984 21.789 1.00 48.56 6 AROM 7022 C THR E 57 71.131 43.984 21.789 1.00 48.33 7 AROM 7025 CA THR E 57 71.131 43.984 21.789 1.00 48.03 6 AROM 7026 CB THR E 57 73.778 46.369 21.796 1.00 48.03 6 AROM 7026 CB THR E 57 73.778 46.369 21.796 1.00 48.03 6 AROM 7026 CB THR E 57 73.789 45.150 20.803 1.00 48.03 6 AROM 7026 CB THR E 57 73.799 45.153 20.803 1.00 49.73 8 AROM 7026 CB THR E 57 73.276 46.369 21.504 1.00 49.73 8 AROM 7026 CB THR E 57 73.799 45.153 20.803 1.00 49.73 8 AROM 7028 CG THR E 57 73.799 45.153 20.803 1.00 49.73 8 AROM 7030 C THR E 57 72.766 43.392 1.00 44.64 7 AROM 7031 N TRP E 58 71.277 46.398 1.488 1.00 47.10 6 AROM 7031 N TRP E 58 71.277 46.398 1.488 1.00 47.10 6 AROM 7031 N TRP E 58 71.277 41.185 11.00 44.64 7 AROM 7031 N TRP E 58 66.834 42.222 17.443 1.00 48.93 6 AROM 7032 CB THR E 57 72.766 48.340 1.590 1.00 41.75 6 AROM 7030 CB THR E 57 72.766 48.340 1.00 49.73 8 AROM 7031 N TRP E 58 66.834 42.222 17.441 1.00 53.54 6 AROM 7031 N TRP E 58 68.834 42.225 1.00 40.939 7 AROM 7031 N TRP E 58 66.834 42.622 17.443 1.00 42.98 6 AROM 7032 CB THR E 58 66.834 42.622 17.443 1.00 42.98 6 AROM 7033 CB THR E 58 66.834 42.622 17.617 1.00 41.25 6 AROM 7030 CB THR E 58 66.834 42.225 11.00 40.00			7007	0	GLN E	54							
ATOM 7011 CG GIN E 55 70.723 47.342 27.257 1.00 57.75 6 ATOM 7012 CG GIN E 55 71.798 47.759 26.296 1.00 65.99 6 ATOM 7013 ORL GIN E 55 71.798 47.759 26.296 1.00 65.99 6 ATOM 7014 NE 2 GIN E 55 73.057 48.745 26.952 1.00 74.02 8 ATOM 7014 NE 2 GIN E 55 73.057 48.637 28.158 1.00 74.02 8 ATOM 7015 C GIN E 55 73.057 48.637 28.158 1.00 74.02 8 ATOM 7016 O GIN E 55 73.057 48.637 28.158 1.00 74.02 8 ATOM 7016 O GIN E 55 69.978 45.446 26.147 1.00 55.16 8 ATOM 7017 N THR E 56 69.370 45.350 24.592 1.00 54.06 6 ATOM 7018 CA THR E 56 69.370 45.350 24.592 1.00 51.47 7 ATOM 7019 CB THR E 56 68.340 43.527 23.323 1.00 48.99 6 ATOM 7021 CG2 THR E 56 68.638 42.228 22.613 1.00 48.99 6 ATOM 7022 C THR E 56 67.621 43.259 24.530 1.00 51.03 8 ATOM 7023 O THR E 56 69.919 45.870 22.374 1.00 48.51 6 ATOM 7024 N THR E 57 71.131 43.984 21.789 1.00 48.51 6 ATOM 7025 CA THR E 57 71.131 43.984 21.789 1.00 48.33 7 ATOM 7026 CB THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7027 OG1 THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7028 CG2 THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7029 C THR E 57 73.079 45.153 20.803 1.00 48.36 6 ATOM 7030 O THR E 57 72.115 43.162 19.688 1.00 47.10 6 ATOM 7030 O THR E 57 72.115 43.162 19.688 1.00 47.10 6 ATOM 7025 CA THR E 57 73.079 45.153 20.803 1.00 48.36 6 ATOM 7026 CB THR E 57 72.115 43.162 19.688 1.00 47.16 8 ATOM 7030 O THR E 57 72.115 43.162 19.688 1.00 47.16 8 ATOM 7030 O THR E 58 72.2766 46.369 21.504 1.00 49.73 8 ATOM 7031 N TRPE 58 72.276 44.309 19.488 1.00 47.16 8 ATOM 7031 CG TRPE 58 69.485 41.463 1.562 1.00 47.16 8 ATOM 7031 CG TRPE 58 69.485 41.463 1.562 1.00 47.16 8 ATOM 7031 CG TRPE 58 69.485 41.463 1.00 45.36 6 ATOM 7031 CG TRPE 58 69.485 41.463 1.00 43.20 6 ATOM 7031 CG TRPE 58 69.485 41.463 1.00 40.00 41.15 6 ATOM 7030 CG TRPE 58 69.485 41.463 1.00 40.00 41.15 6 ATOM 7040 CG TRPE 58 69.485 41.463 1.00 41.00 49.32 6 ATOM 7050 CG TRPE 58 69.485 41.463 1.00 41.00 49.32 6 ATOM 7040 CG TRPE 58 69.485 41.463 1.00 41.00 41.25 6 ATOM 7050 CG ARG E 60 70.690 41.850 1.00 40.00 51.8 6 ATOM 7060 C		MOTA	7008	N	GLN F								
ATOM 7011 CG CLM E 55 71.798 47.759 26.296 1.00 65.99 6 ATOM 7012 CD GLN E 55 72.759 48.467 26.952 1.00 70.08 6 ATOM 7013 OEI GLN E 55 73.057 48.637 28.158 1.00 74.02 8 ATOM 7015 CE GLN E 55 73.057 48.637 28.158 1.00 74.02 8 ATOM 7016 O GLN E 55 69.978 45.466 25.768 1.00 54.06 6 ATOM 7017 N THR E 56 69.370 45.350 24.592 1.00 55.16 8 ATOM 7018 CA THR E 56 69.638 44.266 23.664 1.00 55.16 8 ATOM 7019 CE THR E 56 69.638 44.266 23.664 1.00 49.57 6 ATOM 7020 OEI THR E 56 69.638 44.266 23.664 1.00 49.57 6 ATOM 7021 CG2 THR E 56 69.638 44.266 23.664 1.00 49.57 6 ATOM 7021 CG2 THR E 56 69.919 45.870 22.374 1.00 48.56 6 ATOM 7022 C THR E 56 69.919 45.870 22.374 1.00 48.56 6 ATOM 7024 OEI THR E 57 71.131 43.964 21.916 1.00 47.42 8 ATOM 7025 CA THR E 57 73.778 45.894 21.916 1.00 47.42 8 ATOM 7026 CE THR E 57 73.779 45.153 20.803 1.00 48.33 7 ATOM 7026 CE THR E 57 72.786 46.369 21.504 1.00 49.57 6 ATOM 7028 CE THR E 57 72.786 46.369 21.504 1.00 48.33 7 ATOM 7028 CE THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CE THR E 57 72.786 46.369 21.504 1.00 47.42 8 ATOM 7028 CE THR E 57 72.786 46.369 21.504 1.00 47.10 68 ATOM 7028 CE THR E 57 72.786 46.369 21.504 1.00 47.10 68 ATOM 7031 N TRP E 58 71.217 41.165 17.463 1.00 44.64 7 ATOM 7031 CG THP E 58 72.302 42.272 17.443 1.00 48.33 6 ATOM 7032 CA THR E 57 72.115 43.162 19.688 1.00 47.10 68 ATOM 7033 CD THR E 57 72.786 46.369 21.504 1.00 47.10 68 ATOM 7034 CG THP E 58 69.901 41.550 16.907 1.00 41.75 6 ATOM 7035 CD THP E 58 69.901 41.550 16.907 1.00 41.75 6 ATOM 7036 CD THP E 58 69.901 41.550 16.907 1.00 44.32 6 ATOM 7037 CD THP E 58 69.901 41.550 16.907 1.00 44.32 6 ATOM 7038 CD THP E 58 66.447 43.451 18.347 1.00 45.88 6 ATOM 7034 CG THP E 58 66.447 43.451 18.347 1.00 45.91 8 ATOM 7035 CD THP E 58 69.901 41.550 16.907 1.00 41.05 6 ATOM 7040 CC THP E 58 66.447 43.451 18.347 1.00 46.91 8 ATOM 7040 CC THP E 58 66.447 43.451 18.347 1.00 46.91 8 ATOM 7040 CC THP E 58 66.447 43.451 18.347 1.00 46.91 8 ATOM 7040 CC THP E 58 66.447 43.451 18.347 1.00 46.91 8 ATOM 7040 CC THP E 58 66.	5												
ATOM 7012 CD GIN E 55 73.057 48.745 26.952 1.00 70.80 6 8 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70.00 70													
ATOM 7013 OE1 GLN E 55 73.057 48.637 28.158 1.00 74.02 8 10 ATOM 7014 NE2 GLN E 55 73.245 49.710 26.175 1.00 70.33 7 70.707 7015 C GLN E 55 69.978 45.465 25.768 1.00 54.06 6 10 ATOM 7016 O GLN E 55 69.978 45.465 25.768 1.00 54.06 6 10 ATOM 7017 N THR E 56 69.370 45.350 24.592 1.00 51.47 7 10 ATOM 7018 CA THR E 56 69.638 44.268 23.664 1.00 49.57 6 10 ATOM 7019 CB THR E 56 69.638 44.268 23.664 1.00 49.57 6 10 ATOM 7020 CG1 THR E 56 68.638 42.228 22.613 1.00 48.99 6 ATOM 7021 CG2 THR E 56 68.638 42.228 22.613 1.00 48.99 6 ATOM 7022 C THR E 56 69.919 45.870 21.916 1.00 47.42 8 10 ATOM 7022 C THR E 56 69.919 45.870 21.916 1.00 47.42 8 10 ATOM 7023 O THR E 56 69.919 45.870 21.916 1.00 47.42 8 10 ATOM 7024 C THR E 57 71.778 44.370 20.545 1.00 48.63 6 ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7031 C THR E 57 72.462 42.094 20.196 1.00 47.10 6 ATOM 7031 C THR E 58 71.00 43.337 18.382 1.00 44.64 7 ATOM 7032 C THR E 58 68.834 42.228 1.00 40.04 64 7 ATOM 7034 C THR E 58 68.653 42.622 19.408 1.00 47.10 6 ATOM 7034 C THR E 58 68.653 42.622 19.408 1.00 43.06 6 ATOM 7037 C THR E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7037 C THR E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7037 C THR E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7037 C THR E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7037 C THR E 58 69.901 41.590 16.907 1.00 41.25 6 ATOM 7037 C THR E 58 69.901 41.590 16.907 1.00 41.25 6 ATOM 7037 C THR E 58 69.901 41.590 16.907 1.00 41.25 6 ATOM 7037 C THR E 58 69.901					-								
100 ATOM 7014 NEZ GLN E 55 73.445 49.710 26.175 1.00 70.33 7 ATOM 7017 NO GLN E 55 69.978 45.446 25.768 1.00 54.066 ATOM 7017 NO THE E 55 69.978 45.446 26.147 1.00 55.16 8 ATOM 7017 NO THE E 56 69.370 45.350 24.592 1.00 51.47 7 ATOM 7018 CA THR E 56 69.370 45.350 24.592 1.00 51.47 7 10 ATOM 7019 CB THR E 56 69.370 45.350 24.592 1.00 51.47 7 10 ATOM 7019 CG2 THR E 56 69.370 45.350 24.592 1.00 51.47 7 10 ATOM 7020 OG1 THR E 56 69.384 44.266 23.664 1.00 49.97 6 ATOM 7021 CG2 THR E 56 68.638 42.228 22.613 1.00 48.99 6 ATOM 7021 CG2 THR E 56 69.919 45.870 21.916 1.00 47.42 8 10 ATOM 7022 C THR E 56 69.919 45.870 21.916 1.00 47.42 8 10 ATOM 7023 CD THR E 57 71.131 43.984 21.89 1.00 48.81 6 ATOM 7024 NO THR E 57 71.788 44.370 20.545 1.00 48.63 6 ATOM 7025 CA THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7026 CB THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CCZ THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7028 CCZ THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CCZ THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CCZ THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.786 46.369 21.504 1.00 47.10 6 ATOM 7030 CD THR E 57 72.786 46.369 21.504 1.00 47.10 6 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 48.43 6 ATOM 7031 CB TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7031 CB TRP E 58 69.901 41.590 16.907 1.00 44.32 6 ATOM 7033 CB TRP E 58 69.901 41.590 16.907 1.00 44.32 6 ATOM 7033 CB TRP E 58 69.901 41.590 16.907 1.00 44.32 6 ATOM 7034 CG TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7036 CEZ TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7037 CEZ TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7036 CEZ TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7036 CEZ TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7036 CEZ TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7036 CEZ TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7036 CEZ TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7036 CEZ TRP E 58 69.485 41.463 15.477 1.00 41.32 6													
ATOM 7015 C GLN E 55	10												
ATOM 7016 O GIN E 55 70.834 44.648 26.147 1.00 55.168 8 ATOM 7017 N THER E 56 69.370 45.350 24.592 1.00 51.47 7 ATOM 7018 CA THR E 56 69.638 44.266 23.664 1.00 49.57 6 ATOM 7020 CG1 THR E 56 69.638 44.266 23.664 1.00 49.57 6 ATOM 7021 CG2 THR E 56 67.621 43.259 24.503 1.00 51.03 8 ATOM 7022 C THR E 56 67.621 43.259 24.503 1.00 51.03 8 ATOM 7022 C THR E 56 69.919 45.870 21.916 1.00 48.81 6 ATOM 7022 C THR E 56 69.919 45.870 21.916 1.00 48.56 6 ATOM 7022 C THR E 57 71.131 43.984 21.789 1.00 48.36 6 ATOM 7024 N THR E 57 71.131 43.984 21.789 1.00 48.33 7 ATOM 7025 CA THR E 57 73.079 45.153 20.803 1.00 53.54 6 ATOM 7026 CB THR E 57 73.079 45.153 20.803 1.00 49.73 8 ATOM 7029 C THR E 57 72.165 43.669 21.916 1.00 49.73 8 ATOM 7029 C THR E 57 72.165 43.669 21.916 1.00 47.16 8 ATOM 7030 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7033 CB TRP E 58 69.91 41.590 16.907 1.00 41.25 6 ATOM 7034 CG TRP E 58 69.883 42.272 17.617 1.00 41.75 6 ATOM 7035 CD2 TRP E 58 67.800 42.458 16.669 1.00 47.16 8 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.75 6 ATOM 7037 NET F E 58 68.653 42.227 17.617 1.00 41.75 6 ATOM 7030 NET F E 58 66.553 42.222 17.617 1.00 41.05 6 ATOM 7040 CZ2 TRP E 58 68.653 42.225 17.617 1.00 41.05 6 ATOM 7040 CZ2 TRP E 58 66.553 42.021 19.608 1.00 43.04 6 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 44.04 7 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 44.04 9 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 44.04 9 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 45.83 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 45.83 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 45.83 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 45.83 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 45.83 6 ATOM 7040 CZ2 TRP E 58 67.462 42.225 17.617 1.00 55.98 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 45.83 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 55.98 6 ATOM 7040 CZ2 TRP E 58	10												
ATOM 7017 N THR E 56 69.370 45.350 24.592 1.00 51.47 7 ATOM 7018 CA THR E 56 69.384 44.266 23.664 1.00 49.57 6 ATOM 7019 CB THR E 56 68.384 43.527 23.323 1.00 48.99 6 ATOM 7020 CG1 THR E 56 68.384 43.527 23.323 1.00 48.99 6 ATOM 7021 CG2 THR E 56 67.621 43.259 24.530 1.00 51.03 8 ATOM 7022 C THR E 56 67.621 43.259 24.530 1.00 51.03 8 ATOM 7023 C THR E 56 66.38 42.228 22.613 1.00 48.81 6 ATOM 7023 C THR E 56 69.919 45.870 21.916 1.00 47.42 3 ATOM 7024 N THR E 57 71.131 43.984 21.789 1.00 48.33 7 ATOM 7025 CA THR E 57 71.778 44.370 20.545 1.00 48.33 7 ATOM 7026 CG THR E 57 73.757 45.498 19.488 1.00 49.73 8 ATOM 7027 OG1 THR E 57 72.186 46.369 21.504 1.00 49.73 8 ATOM 7028 CG2 THR E 57 72.185 43.162 19.688 1.00 47.10 6 ATOM 7030 C THR E 57 72.462 42.094 20.196 1.00 47.10 6 ATOM 7031 N TRE 58 77.2.462 42.094 20.196 1.00 47.10 6 ATOM 7032 CA TRP E 58 71.217 41.185 17.463 1.00 45.43 6 ATOM 7035 CA TRP E 58 71.217 41.185 17.463 1.00 44.64 7 ATOM 7036 CG TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7038 CD1 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7038 CD1 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7038 CD2 TRP E 58 68.834 42.225 17.617 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.53 42.622 18.948 1.00 43.06 6 ATOM 7030 CD3 TRP E 58 66.53 42.622 18.948 1.00 43.06 6 ATOM 7040 CZ2 TRP E 58 66.53 42.622 18.948 1.00 43.06 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 43.20 7 ATOM 7040 CZ3 TRP E 58 66.447 43.451 18.347 1.00 43.20 7 ATOM 7040 CZ3 TRP E 58 66.429 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ3 TRP E 58 66.429 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ3 TRP E 58 66.429 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ3 TRP E 58 66.429 41.982 15.477 1.00 43.20 7 ATOM 7050 C SER E 59 72.737 42.039 15.076 1.00 49.99 7 ATOM 7050 C SER E 59 72.737 42.039 15.076 1.00 49.99 7 ATOM 7050 C SER E 59 72.737 42.039 15.076 1.00 49.99 7 ATOM 7050 C SER E 59 72.232 40.640 12.621 1.00 50.23 8 ATOM 7050 C SER E 59 72.232													
ATOM   7018   CA													7
15 ATOM 7010 CB THR E 56 68.340 43.527 23.323 1.00 48.91 6 ATOM 7020 CG1 THR E 56 67.621 43.259 24.530 1.00 48.81 6 ATOM 7021 CC2 THR E 56 68.638 42.228 22.613 1.00 48.81 6 ATOM 7022 C THR E 56 68.638 42.228 22.613 1.00 48.81 6 ATOM 7024 N THR E 56 69.919 45.870 21.916 1.00 47.42 8 ATOM 7025 CA THR E 57 71.131 43.984 21.789 1.00 48.33 7 ATOM 7026 CB THR E 57 71.778 44.370 20.545 1.00 48.33 6 ATOM 7027 CG1 THR E 57 72.786 46.369 21.504 1.00 48.33 6 ATOM 7027 CG1 THR E 57 72.786 46.369 21.504 1.00 47.10 6 ATOM 7030 O THR E 57 72.786 46.369 21.504 1.00 47.10 6 ATOM 7030 O THR E 57 72.786 46.369 21.504 1.00 47.10 6 ATOM 7030 O THR E 57 72.462 42.094 20.196 1.00 47.10 6 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 72.302 42.272 17.443 1.00 44.32 6 ATOM 7033 CB TRP E 58 69.901 41.590 16.907 1.00 44.32 6 ATOM 7036 CE TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7037 CE3 TRP E 58 69.834 42.225 17.617 1.00 43.20 6 ATOM 7037 CE3 TRP E 58 68.834 42.225 17.617 1.00 43.20 6 ATOM 7037 CE3 TRP E 58 68.834 42.225 17.617 1.00 43.20 7 ATOM 7037 CE3 TRP E 58 68.834 42.225 17.617 1.00 43.20 7 ATOM 7030 CC2 TRP E 58 68.834 42.225 17.617 1.00 43.20 7 ATOM 7030 CC3 TRP E 58 68.829 41.982 15.477 1.00 43.20 7 ATOM 7030 CC3 TRP E 58 68.829 41.982 15.477 1.00 43.20 7 ATOM 7040 C22 TRP E 58 66.294 41.982 15.477 1.00 43.20 7 ATOM 7040 C23 TRP E 58 66.294 41.982 15.477 1.00 43.20 7 ATOM 7040 C23 TRP E 58 66.447 43.451 18.347 1.00 46.99 8 ATOM 7040 C23 TRP E 58 66.447 43.451 18.347 1.00 46.99 8 ATOM 7040 C23 TRP E 58 66.447 43.451 18.347 1.00 46.92 6 ATOM 7040 C3 SER E 59 72.332 42.672 17.433 1.00 53.86 6 ATOM 7040 C3 SER E 59 72.933 42.672 17.033 1.00 53.86 6 ATOM 7040 C3 SER E 59 72.934 42.979 15.074 1.00 53.86 6 ATOM 7040 C6 SER E 59 72.934 42.979 15.074 1.00 53.86 6 ATOM 7040 C6 SER E 59 72.934 42.979 15.074 1.00 53.86 6 ATOM 7040 C6 SER E 59 72.934 42.979 15.074 1.00 53.86 6 ATOM 7050 C0 ASP E 60 67.660 41.556 10.743 1.00 59.86 6 ATOM 7050 C0 ASP E 60 67.650 41.757 1.00 61.13 8 ATOM 7050 C0 ASP E 60 67										23.664	1.00	49.57	6
ATOM 7020 CG1 THR E 56 67.621 43.259 24.530 1.00 51.03 8 ATOM 7021 CG2 THR E 56 68.638 42.228 22.613 1.00 48.81 6 ATOM 7022 C THR E 56 69.919 45.870 21.916 1.00 47.42 8  20 ATOM 7023 O THR E 57 71.131 43.984 21.789 1.00 48.36 6 ATOM 7025 CA THR E 57 71.131 43.984 21.789 1.00 48.36 6 ATOM 7026 CB THR E 57 71.778 44.370 20.545 1.00 48.38 6 ATOM 7026 CB THR E 57 72.786 46.369 21.504 1.00 49.73 8  ATOM 7027 CO1 THR E 57 72.786 46.369 21.504 1.00 49.73 8  ATOM 7028 CC2 THR E 57 72.786 46.369 21.504 1.00 49.73 8  ATOM 7030 O THR E 57 72.786 46.369 21.504 1.00 47.10 6 ATOM 7031 N TRP E 58 71.915 40.00 47.10 6 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 47.10 6 ATOM 7032 CA TRP E 58 71.996 43.337 18.382 1.00 47.10 6 ATOM 7033 CB TRP E 58 71.217 41.185 17.463 1.00 47.16 8 ATOM 7033 CB TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7038 CD1 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7039 NEI TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7041 CZ3 TRP E 58 66.447 43.451 1.60 49.98 1.00 42.08 6 ATOM 7041 CZ3 TRP E 58 66.497 43.451 1.00 42.08 6 ATOM 7040 CZ TRP E 58 66.498 43.371 17.00 43.20 7 ATOM 7041 CZ3 TRP E 58 66.498 43.072 17.043 1.00 46.92 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 45.98 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 45.98 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 45.98 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 40.99 8 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 40.99 8 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 40.90 9.89 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 40.90 9.89 6 ATOM 7040 CZ TRP E 58 67.462 43.232 19.301 1.00 42.08 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 40.90 9.89 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 40.90 9.89 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 60.00 1.00 41.95 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 60.00 1.00 41.95 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 60.00 1.00 41.95 6 ATOM 7040 CZ TRP E 58 66.497 43.451 1.00 60.00 1.00 41.90 60.00 60.00 60.00 60.00 60.00 60.00 60.00 60.00 60.00 60.00 60.00 60.	15							68.340	43.527	23.323	1.00	48.99	6
ATOM 7022 C THR E 56 70.245 44.780 22.374 1.00 48.56 6 ATOM 7023 O THR E 56 69.919 45.870 21.916 1.00 47.42 8 ATOM 7025 CA THR E 57 71.131 43.984 21.789 1.00 48.33 7 ATOM 7026 CB THR E 57 71.778 44.370 20.545 1.00 48.33 6 ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 48.38 6 ATOM 7028 CG2 THR E 57 72.786 46.369 21.504 1.00 48.38 6 ATOM 7028 CG2 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CC THR E 57 72.786 46.369 21.504 1.00 47.10 6 ATOM 7030 O THR E 57 72.155 43.162 19.688 1.00 47.10 6 ATOM 7031 N TRP E 58 72.152 43.162 19.688 1.00 47.10 6 ATOM 7031 N TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7032 CA TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7033 CB TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7036 CE2 TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 NOS CD2 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 66.659 42.622 18.948 1.00 42.08 6 ATOM 7040 CZ2 TRP E 58 66.427 43.451 18.347 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.427 43.451 18.347 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.427 43.451 18.347 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.427 43.451 18.347 1.00 42.98 6 ATOM 7040 C TRP E 58 72.450 42.872 17.043 1.00 46.11 6 ATOM 7040 C TRP E 58 72.450 42.872 17.043 1.00 46.92 6 ATOM 7040 C TRP E 58 66.447 43.451 18.347 1.00 46.92 6 ATOM 7040 C TRP E 58 66.447 43.451 18.347 1.00 46.92 6 ATOM 7040 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7040 C TRP E 58 72.450 42.872 16.060 1.00 45.98 6 ATOM 7040 C TRP E 58 66.447 43.451 18.347 1.00 62.88 6 ATOM 7040 C TRP E 58 67.462 43.232 19.301 1.00 45.98 6 ATOM 7040 C TRP E 58 67.477 13.388 12.070 55.16 6 ATOM 7040 C TRP E 58 67.477 13.388 12.070 55.16 6 ATOM 7040 C TRP E 58 67.477 13.388 12.070 55.16 6 ATOM 7040 C TRP E 58 67.477 13.388 12.070 55.16 6 ATOM 7040 C TRP E 58 60 67.600 41.550 10.074 1.00 65.33 7 ATOM 7050 C ASP E 60 60 68.214 41.871 10.00 60.13 8 ATOM 7050 C ASP E 60 60 68.247 41.751 10.00 60.13 8 ATOM 7050 C ASP E 60 60 68.247 41.751 10.00 60.13 8 ATOM 7	. •				THR	E 50	5	67.621	43.259	24.530			
ATOM 7023 O THR E 56 69.919 45.870 21.916 1.00 47.42 8 ATOM 7024 N THR E 57 71.131 43.984 21.789 1.00 48.63 6 ATOM 7025 CA THR E 57 71.778 44.370 20.545 1.00 48.63 6 ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 48.63 6 ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CG THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.115 43.162 19.688 1.00 47.10 6 ATOM 7030 N THR E 57 72.462 42.094 20.196 1.00 47.16 8 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7033 CB TRP E 58 72.302 42.272 17.443 1.00 44.32 6 ATOM 7035 CD2 TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CD2 TRP E 58 67.800 42.458 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 67.800 42.458 16.689 1.00 47.16 6 ATOM 7038 CD1 TRP E 58 67.800 42.458 16.689 1.00 43.06 6 ATOM 7038 CD1 TRP E 58 66.598 43.072 17.00 43.20 7 ATOM 7040 C22 TRP E 58 66.598 43.072 17.00 43.20 7 ATOM 7040 C22 TRP E 58 66.598 43.072 17.00 43.20 7 ATOM 7040 C22 TRP E 58 66.598 43.072 17.00 43.20 7 ATOM 7040 C22 TRP E 58 66.598 43.072 17.00 43.20 7 ATOM 7040 C22 TRP E 58 66.598 43.072 17.00 42.98 6 ATOM 7040 C C72 TRP E 58 66.598 43.072 17.00 42.98 6 ATOM 7040 C C72 TRP E 58 66.598 43.072 17.00 42.98 6 ATOM 7040 C C72 TRP E 58 66.598 43.072 17.00 43.20 7 ATOM 7040 C C72 TRP E 58 66.598 43.072 17.00 42.98 6 ATOM 7040 C C72 TRP E 58 72.450 42.872 16.060 1.00 46.99 8 ATOM 7040 C C72 TRP E 58 72.450 42.872 16.060 1.00 46.99 8 ATOM 7040 C C72 TRP E 58 66.447 43.451 18.347 1.00 62.82 8 ATOM 7040 C C C C C C C C C C C C C C C C C C		ATOM	7021	CG2	THR I	E 56	5	68.638					
20 ATOM 7025 N THR E 57 71.131 43.984 21.789 1.00 48.33 7 ATOM 7025 CA THR E 57 71.778 44.370 20.545 1.00 48.63 6 ATOM 7026 CB THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7027 OG1 THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7028 CG2 THR E 57 73.073 45.498 19.488 1.00 49.73 8 ATOM 7028 CG2 THR E 57 73.073 45.498 19.488 1.00 47.10 6 ATOM 7030 O THR E 57 72.115 43.162 19.688 1.00 47.10 6 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7031 CA TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7033 CB TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7034 CG TRP E 58 69.901 41.550 16.907 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 69.901 41.550 16.907 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7034 CC TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7034 CC TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 10.00 42.08 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 10.00 42.08 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 10.00 42.08 6 ATOM 7040 CZ2 TRP E 58 66.497 43.451 18.347 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.497 43.451 18.347 1.00 49.30 7 ATOM 7040 CA ERE E 59 72.737 42.039 15.076 1.00 49.30 7 ATOM 7040 CA ERE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7040 CA ERE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7040 CA ERE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7040 CA ERE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7040 CA ERE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7040 CA ERE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7040 CA ERE E 59 72.933 42.571 13.3382 1.00 55.16 6 ATOM 7040 CA ERE E 59 72.933 42.571 1.00 60.05 8.86 6 ATOM 7040 CA ARG E 60 60.614 42.206 10.743 1.00 59.89 8 6 ATOM 7050 CA ARG E 60 60.614 42.206 10.743 1.00 59.89 8 6 AT		ATOM	7022	С	THR :	E 56	5						
ATOM 7026 CA THR E 57 71.778 44.370 20.545 1.00 48.63 6 ATOM 7026 CB THR E 57 73.079 45.153 20.803 1.00 48.33 6 ATOM 7027 CG1 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CG2 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7029 C THR E 57 72.115 43.162 19.688 1.00 47.16 8 ATOM 7030 O THR E 57 72.415 43.162 19.688 1.00 47.16 8 ATOM 7031 N TRP E 58 72.302 42.272 17.443 1.00 44.64 7 ATOM 7032 CA TRP E 58 72.302 42.272 17.443 1.00 44.32 6 ATOM 7033 CB TRP E 58 71.217 41.185 17.463 1.00 44.32 6 ATOM 7035 CD2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7036 CE2 TRP E 58 67.800 42.458 16.689 1.00 47.75 6 ATOM 7037 CB3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 69.948 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.598 41.963 15.622 1.00 39.77 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 45.88 6 ATOM 7040 CZ2 TRP E 58 67.460 42.3232 19.301 1.00 44.98 6 ATOM 7040 CZ2 TRP E 58 67.460 43.323 17.00 42.98 6 ATOM 7040 CZ2 TRP E 58 72.312 44.079 15.874 1.00 45.88 6 ATOM 7040 CZ2 TRP E 58 72.450 42.872 16.060 1.00 46.99 8 ATOM 7040 CZ2 TRP E 58 72.450 42.872 16.060 1.00 46.99 8 ATOM 7040 CZ TRP E 58 72.450 42.872 16.060 1.00 46.99 8 ATOM 7040 CZ TRP E 58 72.312 44.079 15.874 1.00 46.99 8 ATOM 7040 CZ TRP E 58 72.450 42.872 16.060 1.00 46.99 8 ATOM 7047 CZ SRE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7047 CZ SRE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7047 CZ SRE E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7047 CZ SRE E 59 72.033 41.873 12.673 1.00 53.08 8 ATOM 7040 CZ SRE E 59 72.033 41.873 12.673 1.00 53.08 8 ATOM 7050 O SER E 59 72.033 41.873 12.673 1.00 53.08 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.027 1.00 53.08 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.027 1.00 62.82 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.027 1.00 60.13 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.027 1.00 62.81 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.027 1.00 62.81 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.027 1.00 62.81 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.027 1.00 62.81 8 ATOM 7050 CA ASP E 60 69.1		ATOM	7023	0									
ATOM 7026 CB THR E 57 73.079 45.153 20.803 1.00 48.38 6 ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CG2 THR E 57 73.737 45.498 19.488 1.00 53.54 6 ATOM 7030 O THR E 57 72.115 43.162 19.688 1.00 47.10 6 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 47.16 8 ATOM 7032 CA TRP E 58 71.996 43.337 18.382 1.00 44.34 6 ATOM 7033 CB TRP E 58 71.217 41.185 17.463 1.00 45.43 6 ATOM 7034 CG TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CC2 TRP E 58 68.834 42.225 17.617 1.00 41.75 6 ATOM 7037 CE3 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7038 CD1 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7039 NEI TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.08 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.447 43.232 19.301 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 44.99 6 ATOM 7043 C TRP E 58 72.312 44.079 15.874 1.00 42.98 6 ATOM 7043 C TRP E 58 72.312 44.079 15.874 1.00 42.98 6 ATOM 7043 C TRP E 58 72.312 44.079 15.874 1.00 42.98 6 ATOM 7046 CA SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7049 C SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7049 C SER E 59 72.933 42.571 13.338 1.00 55.16 6 ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 55.39 7 ATOM 7050 C SER E 59 72.093 41.873 12.673 1.00 55.39 7 ATOM 7050 C SER E 59 72.093 41.873 12.673 1.00 55.39 7 ATOM 7050 C SER E 59 72.093 41.873 12.673 1.00 55.39 7 ATOM 7050 C SER E 60 67.060 41.556 10.074 1.00 66.18 6 ATOM 7057 C ASP E 60 67.060 41.556 10.074 1.00 66.18 6 ATOM 7058 O ASP E 60 67.060 41.556 10.074 1.00 66.18 6 ATOM 7057 C ASP E 60 67.060 41.556 10.074 1.00 66.18 6 ATOM 7050 C ASP E 60 67.060 41.556 10.074 1.00 66.18 6 ATOM 7050 C ASP E 60 67.060 41.556 10.074 1.00 66.18 6 ATOM 7050 C ASP E 60 67.060 41.556 10.074 1.00 66.18 6 ATOM 7051 CB ARG E 61 77.411 41.855 7.223 1.00 60.38 6	20	MOTA											
ATOM 7027 OG1 THR E 57 72.786 46.369 21.504 1.00 49.73 8 ATOM 7028 CG2 THR E 57 73.737 45.498 19.488 1.00 53.54 6 ATOM 7029 C THR E 57 72.115 43.162 19.688 1.00 47.10 6 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7033 CB TRP E 58 71.217 41.185 17.463 1.00 44.32 6 ATOM 7034 CG TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7035 CD2 TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7039 NEI TRP E 58 68.29 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 43.20 7 ATOM 7041 CZ3 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 46.91 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 46.99 8 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 46.99 8 ATOM 7040 CZ2 TRP E 58 72.312 44.079 15.874 1.00 46.99 8 ATOM 7046 CA SER E 59 72.373 42.039 15.076 1.00 49.39 7 ATOM 7048 CG SER E 59 72.433 42.571 13.738 1.00 55.16 6 ATOM 7048 CG SER E 59 72.933 42.571 13.738 1.00 55.86 6 ATOM 7050 O SER E 59 72.933 42.571 13.738 1.00 55.86 6 ATOM 7051 N ASP E 60 67.060 41.875 1.034 1.00 58.89 6 ATOM 7050 O SER E 59 72.933 42.571 13.738 1.00 55.86 6 ATOM 7051 N ASP E 60 67.060 41.875 1.00 59.87 6 ATOM 7050 CSE E 59 72.933 42.571 13.738 1.00 55.89 7 ATOM 7051 N ASP E 60 68.214 41.871 10.00 6.100 6.053 8 ATOM 7052 CA ASP E 60 67.060 41.556 10.374 1.00 66.18 6 ATOM 7053 CB ASP E 60 67.060 41.556 10.374 1.00 66.18 6 ATOM 7050 CD ASP E 60 67.060 41.556 10.374 1.00 66.18 6 ATOM 7051 CB ARG E 61 73.580 42.555 6.908 1.00 70.24 6 ATOM 7052 CG ASP E 60 67.059 44.106 9.293 1.00 60.13 8 ATOM 7053 CB ASP E 60 67.060 41.556 6.908 1.00 70.24 6 ATOM 7050 CB ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7050 CD ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7050 CB ASP E 60 67.060 41.556 6.908 1.00 70.418 6 ATOM 7050 CB ASP E 60 67.060 41.556 6.90													
ATOM 7028 CG2 THR E 57 73.737 45.498 19.488 1.00 53.54 6 ATOM 7029 C THR E 57 72.462 42.094 20.196 1.00 47.16 8 ATOM 7030 O THR E 57 72.462 42.094 20.196 1.00 47.16 8 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 72.462 42.094 20.196 1.00 47.16 8 ATOM 7033 CB TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7033 CB TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7034 CG TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7035 CD2 TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.8653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 68.66.533 42.622 18.948 1.00 42.08 6 ATOM 7039 NE1 TRP E 58 68.292 41.982 15.477 1.00 43.06 6 ATOM 7040 CZ2 TRP E 58 666.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 666.598 43.072 17.043 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 666.447 43.451 18.347 1.00 45.88 6 ATOM 7042 CH2 TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7043 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7049 C SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7049 C SER E 59 72.933 42.571 13.738 1.00 55.16 6 ATOM 7049 C SER E 59 72.023 40.640 12.621 1.00 53.08 6 ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 53.08 6 ATOM 7051 N ASP E 60 69.144 42.502 11.027 1.00 53.08 6 ATOM 7052 CA ASP E 60 69.144 42.502 11.027 1.00 53.08 6 ATOM 7055 CD1 ASP E 60 68.214 1.701 8.835 1.00 59.85 8 ATOM 7055 CD1 ASP E 60 68.224 11.701 8.835 1.00 59.85 8 ATOM 7057 C ASP E 60 67.060 41.556 10.374 1.00 66.18 6 ATOM 7058 O ASP E 60 70.059 44.106 9.293 1.00 60.13 8 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7056 CD2 ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7056 CD2 ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7056 CD2 ASR E 61 73.580 42.155 6.908 1.00 70.41 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.41 6													
25 ATOM 7029 C THR E 57 72.115 43.162 19.688 1.00 47.10 6 ATOM 7030 O THR E 57 72.462 42.094 20.196 1.00 47.10 6 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7034 CG TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7035 CD2 TRP E 58 68.834 42.252 17.617 1.00 41.75 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 43.06 6 ATOM 7037 CE3 TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7037 CE3 TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.447 43.451 18.347 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.447 43.451 18.347 1.00 45.88 6 ATOM 7042 CH2 TRP E 58 72.450 42.872 16.060 1.00 49.39 7 ATOM 7044 C TRP E 58 72.450 42.872 16.060 1.00 49.39 7 ATOM 7044 C TRP E 58 72.450 42.872 16.060 1.00 49.39 7 ATOM 7047 CB SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7047 CB SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7047 CB SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7048 OG SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7048 OG SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7050 O SER E 59 72.933 42.571 13.738 1.00 59.85 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7050 C ASP E 60 68.224 41.871 10.006 1.00 61.83 6 ATOM 7057 C ASP E 60 68.224 41.871 10.006 1.00 61.83 6 ATOM 7057 C ASP E 60 68.224 41.871 10.006 1.00 61.33 6 ATOM 7057 C ASP E 60 69.144 42.505 11.007 1.00 62.51 8 ATOM 7050 C ASP E 60 67.060 41.556 10.374 1.00 62.51 8 ATOM 7057 C ASP E 60 67.060 41.556 10.374 1.00 62.51 8 ATOM 7057 C ASP E 60 67.060 41.556 10.374 1.00 62.51 8 ATOM 7050 C ASP E 60 67.060 41.556 10.374 1.00 62.51 8 ATOM 7057 C ASP E 60 67.060 41.556 69.98 1.00 60.13 8 ATOM 7050 C ASP E 60 67.060 41.556 69.98 1.00 60.13 8 ATOM 7060 CA ARG E 61 71.942 82.989 7.													
ATOM 7030 O THR E 57 72.462 42.094 20.196 1.00 47.16 8 ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7033 CB TRP E 58 72.302 42.272 17.443 1.00 44.64 7 ATOM 7035 CB TRP E 58 72.302 42.272 17.443 1.00 44.32 6 ATOM 7036 CB TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7036 CE2 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 68.229 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7042 CT2 TRP E 58 66.447 43.451 18.347 1.00 45.88 6 ATOM 7043 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7046 CA SER E 59 72.331 44.079 15.874 1.00 46.92 6 ATOM 7046 CA SER E 59 72.333 42.571 13.382 1.00 52.86 6 ATOM 7047 CB SER E 59 72.933 42.571 13.382 1.00 52.86 6 ATOM 7049 C SER E 59 72.933 42.571 13.382 1.00 52.86 6 ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 59.85 8 ATOM 7050 O SER E 59 72.033 41.873 12.673 1.00 55.39 7 ATOM 7050 C SER E 59 72.023 40.640 12.621 1.00 59.85 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.037 1.00 59.87 6 ATOM 7050 CA ASP E 60 69.144 42.502 11.071 1.00 61.07 6 ATOM 7050 CA ASP E 60 69.144 42.502 11.00 50.22 8 ATOM 7050 CA ASP E 60 69.144 42.502 11.00 59.87 6 ATOM 7050 CA ASP E 60 69.144 42.502 11.00 59.87 6 ATOM 7050 CA ASP E 60 69.144 42.502 11.00 61.00 61.07 6 ATOM 7050 CA ASP E 60 69.144 42.502 11.00 61.03 61.83 6 ATOM 7050 CA ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 CA ARG E 61 71.946 42.359 7.501 1.00 61.373 7 ATOM 7060 CA ARG E 61 71.946 42.359 7.501 1.00 66.18 6 ATOM 7060 CA ARG E 61 72.428 42.999 7.501 1.00 66.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 70.24 6	05												
ATOM 7031 N TRP E 58 71.996 43.337 18.382 1.00 44.64 7 ATOM 7032 CA TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7033 CB TRP E 58 71.217 41.185 17.463 1.00 44.32 6 ATOM 7034 CG TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7035 CD2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7039 NE1 TRP E 58 68.6598 43.072 17.043 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.447 43.451 18.347 1.00 42.98 6 ATOM 7042 CH2 TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7045 N SER E 59 72.312 44.079 15.874 1.00 46.99 8 ATOM 7046 CA SER E 59 74.423 42.477 13.362 1.00 55.16 6 ATOM 7048 OG SER E 59 74.477 43.368 12.335 1.00 59.85 8 ATOM 7049 C SER E 59 74.477 43.368 12.335 1.00 59.85 8 ATOM 7050 C SER E 59 72.033 40.640 12.621 1.00 59.87 6 ATOM 7050 C SER E 59 72.033 40.640 12.621 1.00 59.87 6 ATOM 7050 C SER E 59 72.033 40.640 12.621 1.00 59.87 6 ATOM 7050 C SER E 59 72.033 40.640 12.621 1.00 59.87 6 ATOM 7050 C SER E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7050 C SER E 60 71.461 42.685 11.833 1.00 59.85 8 ATOM 7050 C SER E 60 71.461 42.685 11.833 1.00 59.85 8 ATOM 7050 C SER E 60 71.461 42.685 11.833 1.00 59.85 8 ATOM 7050 C SER E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7050 C SER E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 C SER E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 C SER E 60 70.616 42.206 10.743 1.00 63.73 7 ATOM 7050 C SER E 60 70.614 42.975 9.508 1.00 63.73 7 ATOM 7050 C SER E 60 70.599 44.106 9.293 1.00 63.73 7 ATOM 7050 C SER E 60 70.599 44.106 9.293 1.00 63.73 7 ATOM 7050 C SER E 60 70.599 44.106 9.293 1.00 63.73 7 ATOM 7050 C ASP E 60 70.616 42.206 10.743 1.00 63.73 7 ATOM 7050 C ASP E 60 70.616 42.206 10.743 1.00 63.73 7 ATOM 7050 C ASP E 60 70.616 42.206 10.743 1.00 63.73 7 ATOM 7050 C ASP E 60 71.041 42.975 9.508 1.00 60.13 8 ATOM 7051 C ASP E 60 71.041 42.975 9.508 1.00 60.	20												
ATOM 7032 CA TRP E 58 72.302 42.272 17.443 1.00 45.43 6 ATOM 7033 CB TRP E 58 71.217 41.185 17.463 1.00 44.32 6 ATOM 7034 CG TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7035 CDZ TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7036 CE2 TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7039 NE1 TRP E 58 68.229 41.982 15.477 1.00 43.20 7 ATOM 7040 CZZ TRP E 58 66.598 33.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.447 43.451 18.347 1.00 45.88 6 ATOM 7042 CH2 TRP E 58 66.447 43.451 18.347 1.00 46.91 6 ATOM 7045 N SER E 59 72.312 44.079 15.874 1.00 46.99 8 ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 52.86 6 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 59.85 8 ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 59.85 8 ATOM 7050 C ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7050 C ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7050 CD ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7050 CD ASP E 60 69.144 42.975 9.508 1.00 62.82 8 ATOM 7050 CD ASP E 60 67.060 41.556 11.037 1.00 62.82 8 ATOM 7050 CD ASP E 60 67.060 41.556 11.037 1.00 62.82 8 ATOM 7050 CD ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 CD ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 CD ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 CD ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 CD ASP E 60 70.599 44.106 9.293 1.00 61.07 6 ATOM 7050 CD ASP E 60 70.599 44.106 9.293 1.00 61.07 6 ATOM 7050 CD ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 63.73 7 ATOM 7060 CA ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7060 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6													7
ATOM 7033 CB TRP E 58 69.901 41.185 17.463 1.00 44.32 6 ATOM 7034 CG TRP E 58 69.901 41.590 16.907 1.00 41.75 6 ATOM 7036 CEZ TRP E 58 68.834 42.225 17.617 1.00 41.25 6 ATOM 7036 CEZ TRP E 58 67.800 42.458 16.689 1.00 43.06 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7039 NE1 TRP E 58 68.299 41.982 15.477 1.00 43.20 7 ATOM 7040 CZZ TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7042 CH2 TRP E 58 66.447 43.451 18.347 1.00 46.92 8 ATOM 7044 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7045 N SER E 59 72.312 44.079 15.874 1.00 46.99 8 ATOM 7046 CA SER E 59 72.312 44.079 15.874 1.00 46.99 8 ATOM 7047 CB SER E 59 74.473 42.039 15.076 1.00 49.39 7 ATOM 7048 OG SER E 59 74.473 42.039 15.076 1.00 49.39 7 ATOM 7048 OG SER E 59 74.477 43.368 12.335 1.00 55.16 6 ATOM 7050 N SER E 59 74.477 43.368 12.335 1.00 55.86 6 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7050 CB ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 CB ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7050 CB ASP E 60 70.699 44.106 9.293 1.00 60.13 8 ATOM 7050 CB ASP E 60 70.699 44.106 9.293 1.00 60.13 8 ATOM 7050 CB ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7050 CB ARG E 61 72.428 42.989 7.501 1.00 63.73 7 ATOM 7060 CA ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6											1.00	45.43	6
SO									41.185	17.463	1.00	44.32	6
ATOM 7036 CE2 TRP E 58 67.800 42.458 16.689 1.00 43.06 6 ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7039 NE1 TRP E 58 68.229 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.447 43.451 18.347 1.00 46.11 6 ATOM 7042 CH2 TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.92 6 ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.99 8 ATOM 7046 CA SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7046 CA SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7048 OG SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7048 OG SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 59.85 8 ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 59.85 8 ATOM 7050 O SER E 59 72.093 40.640 12.621 1.00 50.22 8 ATOM 7050 C SER E 59 72.093 40.640 12.621 1.00 50.22 8 ATOM 7050 C SER E 60 70.616 42.206 10.743 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 59.87 6 ATOM 7055 OD1 ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7057 C ASP E 60 70.606 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 70.599 44.106 92.93 1.00 60.13 8 ATOM 7050 O ARG E 61 70.44 42.975 9.508 1.00 61.07 6 ATOM 7050 O ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7050 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 74.18 6 ATOM 7063 CD ARG E 61 77.411 41.855 7.223 1.00 86.19 7	30						В	69.901	41.590	16.907			
ATOM 7037 CE3 TRP E 58 68.653 42.622 18.948 1.00 42.08 6 ATOM 7038 CD1 TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7039 NE1 TRP E 58 68.229 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 66.447 43.451 18.347 1.00 45.88 6 ATOM 7042 CH2 TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.92 6 ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7049 C SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 59.85 8 ATOM 7050 C SER E 59 72.023 40.640 12.621 1.00 59.85 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7055 CD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7057 C ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7058 O ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7050 C ASP E 60 70.616 42.206 10.743 1.00 59.87 6 ATOM 7055 CD2 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7057 C ASP E 60 70.599 44.106 9.293 1.00 61.83 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 61.33 7 ATOM 7050 C ASP E 60 70.599 44.106 9.293 1.00 61.13 8 ATOM 7050 C ASP E 60 70.599 44.106 9.293 1.00 61.13 8 ATOM 7050 C ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7050 C A ARG E 61 72.428 42.989 7.501 1.00 60.13 8 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 74.18 6 ATOM 7062 CG ARG E 61 73.580 42.155 6.908 1.00 74.18 6 ATOM 7063 CD ARG E 61 77.411 41.855 7.223 1.00 80.58 6		MOTA	7035	CD2	TRP	E 5	В						
ATOM 7038 CD1 TRP E 58 69.485 41.463 15.622 1.00 39.77 6 ATOM 7039 NE1 TRP E 58 68.229 41.982 15.477 1.00 43.20 7 ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 67.462 43.232 19.301 1.00 45.88 6 ATOM 7042 CH2 TRP E 58 66.447 43.451 18.347 1.00 46.11 6 ATOM 7043 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.99 8 ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7046 CA SER E 59 72.933 42.571 13.382 1.00 52.86 6 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7048 OG SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7040 C SER E 59 72.093 41.873 12.673 1.00 59.85 8 45 ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 59.85 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7056 OD2 ASP E 60 68.214 41.871 10.006 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 62.51 8 ATOM 7058 O ASP E 60 70.616 42.205 10.374 1.00 62.82 8 ATOM 7056 OD2 ASP E 60 71.041 42.975 9.508 1.00 62.51 8 ATOM 7056 CA ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7050 CA ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7050 CA ARG E 61 71.896 42.351 8.701 1.00 66.18 6 ATOM 7050 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6		MOTA		CE2									
STOM													
ATOM 7040 CZ2 TRP E 58 66.598 43.072 17.043 1.00 42.98 6 ATOM 7041 CZ3 TRP E 58 67.462 43.232 19.301 1.00 45.88 6 ATOM 7042 CH2 TRP E 58 66.447 43.451 18.347 1.00 46.11 6 ATOM 7043 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.99 8 ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7046 CA SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7047 CB SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 59.85 8  45 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 59.85 8 ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 50.22 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 50 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 70.599 44.106 9.293 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8 55 ATOM 7050 CA ARG E 61 71.896 42.351 8.701 1.00 62.82 8 ATOM 7061 CB ARG E 61 72.428 42.989 7.501 1.00 60.13 8 ATOM 7061 CB ARG E 61 72.428 42.989 7.501 1.00 60.18 6 ATOM 7061 CB ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6	0.5												
ATOM 7041 CZ3 TRP E 58 67.462 43.232 19.301 1.00 45.88 6 ATOM 7042 CH2 TRP E 58 66.447 43.451 18.347 1.00 46.11 6 ATOM 7043 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6 ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.99 8 ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7046 CA SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 52.86 6 ATOM 7048 OG SER E 59 74.777 43.368 12.335 1.00 59.85 8 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 59.85 8 ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 50.22 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 62.51 8 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7050 CB ARG E 61 73.580 42.351 8.701 1.00 66.18 6 ATOM 7060 CA ARG E 61 73.580 42.155 6.998 1.00 70.24 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.998 1.00 70.24 6 ATOM 7063 CD ARG E 61 73.580 42.155 6.998 1.00 70.24 6 ATOM 7063 CD ARG E 61 73.580 42.155 6.998 1.00 70.24 6 ATOM 7063 CD ARG E 61 73.580 42.155 6.998 1.00 70.24 6 ATOM 7063 CD ARG E 61 73.580 42.155 6.998 1.00 74.18 6 ATOM 7063 CD ARG E 61 73.580 42.155 6.998 1.00 74.18 6 ATOM 7063 CD ARG E 61 73.580 42.155 6.998 1.00 74.18 6 ATOM 7063 CD ARG E 61 73.580 42.155 6.998 1.00 74.18 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 77.411 41.855 7.223 1.00 80.58 6	35												
ATOM 7042 CH2 TRP E 58 66.447 43.451 18.347 1.00 46.11 6 ATOM 7043 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6  ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.99 8  ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7  ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6  ATOM 7047 CB SER E 59 74.777 43.368 12.335 1.00 55.16 6  ATOM 7048 OG SER E 59 74.777 43.368 12.335 1.00 59.85 8  45 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 53.08 6  ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 50.22 8  ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7  ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6  ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6  ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6  ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8  ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8  ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 62.51 8  ATOM 7058 O ASP E 60 71.041 42.975 9.508 1.00 62.51 8  ATOM 7050 CB ARG E 61 72.428 42.989 7.501 1.00 66.18 6  ATOM 7061 CB ARG E 61 72.428 42.989 7.501 1.00 66.18 6  ATOM 7062 CG ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7063 CD ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7063 CD ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7063 CD ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6  ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6  ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6													
ATOM 7043 C TRP E 58 72.450 42.872 16.060 1.00 46.92 6  ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.99 8  ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7  ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6  ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 55.16 6  ATOM 7048 OG SER E 59 74.777 43.368 12.335 1.00 55.16 6  ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 53.08 6  ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 53.08 6  ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7  ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6  ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6  50 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6  ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8  ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6  ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 63.73 7  ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7  ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 63.73 7  ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7063 CD ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6  ATOM 7063 CD ARG E 61 77.411 41.855 7.223 1.00 80.58 6													
40 ATOM 7044 O TRP E 58 72.312 44.079 15.874 1.00 46.99 8 ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7048 OG SER E 59 74.777 43.368 12.335 1.00 59.85 8  45 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 53.08 6 ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 50.22 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6  50 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7057 C ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7058 O ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7060 CA ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6										16.060			6
ATOM 7045 N SER E 59 72.737 42.039 15.076 1.00 49.39 7 ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7048 OG SER E 59 74.777 43.368 12.335 1.00 59.85 8 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 53.08 6 ATOM 7050 O SER E 59 72.093 41.873 12.673 1.00 53.08 6 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 55.39 7 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7055 OD1 ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD2 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.51 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 66.13 8 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 77.411 41.855 7.223 1.00 80.58 6	40								44.079	15.874	1.00	46.99	8
ATOM 7046 CA SER E 59 72.933 42.571 13.738 1.00 52.86 6 ATOM 7047 CB SER E 59 74.423 42.477 13.382 1.00 55.16 6 ATOM 7048 OG SER E 59 74.777 43.368 12.335 1.00 59.85 8  45 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 53.08 6 ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 50.22 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 63.73 7 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6				N	SER	E 5	9	72.737	42.039	15.076			
ATOM 7048 OG SER E 59 74.777 43.368 12.335 1.00 59.85 8  ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 53.08 6  ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 50.22 8  ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7  ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6  ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6  ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6  ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8  ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8  ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6  ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7  ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6  ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6  ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6		MOTA		CA	SER	E 5	9						
45 ATOM 7049 C SER E 59 72.093 41.873 12.673 1.00 53.08 6 ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 50.22 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6		ATOM	7047	CB									
ATOM 7050 O SER E 59 72.023 40.640 12.621 1.00 50.22 8 ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6				OG									
ATOM 7051 N ASP E 60 71.461 42.685 11.833 1.00 55.39 7 ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6	45												
ATOM 7052 CA ASP E 60 70.616 42.206 10.743 1.00 58.98 6 ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6													
ATOM 7053 CB ASP E 60 69.144 42.502 11.027 1.00 59.87 6 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7063 CD ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6													
50 ATOM 7054 CG ASP E 60 68.214 41.871 10.006 1.00 61.83 6 ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6													
ATOM 7055 OD1 ASP E 60 68.625 41.701 8.835 1.00 62.51 8 ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6  60 ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7	50												
ATOM 7056 OD2 ASP E 60 67.060 41.556 10.374 1.00 62.82 8 ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6 ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7	00										1.00	62.51	
ATOM 7057 C ASP E 60 71.041 42.975 9.508 1.00 61.07 6 ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7  ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6  ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6  ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6  ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7													
ATOM 7058 O ASP E 60 70.599 44.106 9.293 1.00 60.13 8  ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7  ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6  ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6  ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6  ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6  ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7							0	71.041	42.975		-		
55 ATOM 7059 N ARG E 61 71.896 42.351 8.701 1.00 63.73 7 ATOM 7060 CA ARG E 61 72.428 42.989 7.501 1.00 66.18 6 ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6 60 ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7					ASP								
ATOM 7061 CB ARG E 61 73.580 42.155 6.908 1.00 70.24 6 ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6  ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7	55	MOTA											
ATOM 7062 CG ARG E 61 74.957 42.308 7.596 1.00 74.18 6 ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6 60 ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7													
ATOM 7063 CD ARG E 61 76.042 41.679 6.722 1.00 80.58 6 60 ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7													
60 ATOM 7064 NE ARG E 61 77.411 41.855 7.223 1.00 86.19 7													
00 Alon 7001 Hz tato = 1	80												
	30												

PCT/EP01/01457

WO 01/58951

						-188				,
	MOTA	7066	NH1.	ARG E	61	78.383	40.734	5.447	1.00 88.94	7
	ATOM	7067		ARG E		79.724	41.603	7.111	1.00 88.58	7
	ATOM	7068		ARG E		71.404	43.289	6.414	1.00 65.48	б
	ATOM	7069	_	ARG E		71.655	44.145	5.561	1.00 65.84	8
5	ATOM	7070		THR E		70.255	42.610	6.439	1.00 64.00	7
3	ATOM	7071		THR E		69.232	42.842	5.410	1.00 61.93	6
	MOTA	7072		THR E		68.113	41.764	5.439	1.00 62.28	6
		7072		THR E		67.367	41.879	6.652	1.00 65.24	8
	MOTA	7074		THR E		68.707	40.361	5.372	1.00 61.73	6
10	MOTA MOTA	7075		THR E		68.602	44.218	5.595	1.00 59.03	6
10		7076		THR E		67.827	44.676	4.761	1.00 57.27	8
	MOTA MOTA	7077	N	LEU E		68.962	44.868	6.697	1.00 57.62	7
	ATOM	7078		LEU E		68.461	46.200	7.029	1.00 57.37	6
	ATOM	7079		LEU E		68.214	46.316	8.543	1.00 55.66	6
15		7089		LEU E		67.253	45.322	9.196	1.00 55.07	6
13	MOTA	7080		LEU E		67.231	45.508	10.692	1.00 52.03	6
	MOTA MOTA	7081		LEU E		65.875	45.519	8.612	1.00 55.09	6
		7082	C	LEU E		69.471	47.277	6.625	1.00 57.97	6
	MOTA	7083	0	LEU E		69.135	48.460	6.549	1.00 56.59	8
20	ATOM ATOM	7084	Ŋ	ALA E		70.715	46.862	6.389	1.00 58.86	7
20		7085	CA	ALA E		71.770	47.798	6.018	1.00 60.30	6
	MOTA	7085	CB	ALA E		73.077	47.055	5.844	1.00 58.52	6
	MOTA	7087	C	ALA E		71.440	48.571	4.745	1.00 61.25	6
	MOTA	7089	0	ALA E		70.814	48.041	3.830	1.00 59.01	8
25	MOTA	7099	Ŋ	TRP I		71.845	49.832	4.702	1.00 63.42	7
20	MOTA MOTA	7090	CA	TRP E		71.619	50.631	3.514	1.00 67.05	6
	MOTA	7091	CB	TRP I		70.406	51.537	3.704	1.00 66.45	6
	MOTA	7092	CG	TRP I		70.513	52.506	4.835	1.00 66.84	6
	MOTA	7093		TRP I		70.173	52.266	6.209	1.00 67.35	6
30		7095	CE2			70.352	53.488	6.904	1.00 67.71	6
30	ATOM ATOM	7096	CE3			69.730	51.141	6.920	1.00 65.56	6
	ATOM	7090		TRP I		70.882	53.816	4.756	1.00 66.32	6
	ATOM	7098		TRP		70.785	54.415	5.993	1.00 67.91	7
	ATOM	7099		TRP		70.101	53.615	8.270	1.00 65.59	6
35	ATOM	7100	CZ3			69.483	51.267	8.272	1.00 64.14	6
00	ATOM	7101		TRP		69.668	52.497	8.935	1.00 65.02	6
	ATOM	7102	C	TRP		72.874	51.449	3.253	1.00 69.81	6
	ATOM	7103	Ö	TRP		73.908	51,237	3.902	1.00 70.35	8
	ATOM	7103	N	ASN		72.801	52.370	2.297	1.00 71.64	7
40	ATOM	7105	CA	ASN		73.956	53.203	1.999	1.00 72.49	6
70	ATOM	7106	СВ	ASN		74.174	53.318	0.486	1.00 73.41	6
	ATOM	7107		ASN		75.497	53.990	0.131	1.00 75.13	6
	ATOM	7108		ASN	E 66	75.513	55.081	-0.456	1.00 76.49	8
	ATOM	7109		ASN		76.614	53.347	0.487	1.00 73.59	7
45	MOTA	7110	C	ASN		73.707	54.561	2.602	1.00 72.73	6
	ATOM	7111	ō	ASN		72.930	55.361	2.068	1.00 72.23	8
	ATOM	7112	N	SER		74.367	54.810	3.726	1.00 74.00	7
	MOTA	7113	CA	SER		74.231	56.076	4.441	1.00 76.61	6
	ATOM	7114		SER		74.159	55.805	5.942	1.00 76.40	6
50	ATOM	7115		SER		75.161	54.878	6.307	1.00 75.84	8
•	ATOM	7116		SER		75.378	57.041	4.150	1.00 78.08	6
	MOTA	7117		SER		75.512	58.093	4.807	1.00 77.79	8
	ATOM	7118		SER		76.199	56.678	3.162	1.00 79.24	7
	MOTA	7119		SER		77.353	57.486	2.769	1.00 79.93	6
55	MOTA	7120		SER		78.217	56.734	1.730	1.00 80.16	6
-	ATOM	7121		SER		77.535	56.523	0.495	1.00 81.02	8
	ATOM	7122		SER		76.896		2.219		6
	MOTA	7123		SER		77.586		1.411		8
	MOTA	7124		HIS		75.722	59.261	2.664		7
60	MOTA	7125		HIS		75.176		2.247		6
	ATOM	7126		HIS		75.229	60.665	0.732	1.00 76.74	6

WO 01/58951 PCT/EP01/01457

							-189	·			
	ATOM	7127	CG	HIS E	69		75.366	62.083	0.283	1.00 77.46	6
	ATOM	7128		HIS E	69		74.568	62.857	-0.491	1.00.76.01	6
	ATOM	7129		HIS E	69		76.390	62.898	0.720	1.00 75.50	7
	ATOM	7130		HIS E	69		76.212	64.114	0.239	1.00 74.91	6
5	ATOM	7131		HIS E	69		75.115	64.117	-0.497	1.00 77.04	7
3	ATOM	7132		HIS E	69		73.748	60.641	2.716	1.00 75.96	6
	ATOM	7132		HIS E	69		72.954	61.408	2.170	1.00 75.96	8
	ATOM	7134	И	SER E	70	•	73,431	59,880	3.754	1.00 75.27	7
	ATOM	7135	CA	SER E	70		72.086	59.867	4.308	1.00 72.77	6
10	ATOM	7136	CB	SER E	70		71.307	58.758	3.639	1.00 71.14	6
10	ATOM	7137	OG	SER E	70		72.085	57.578	3.703	1.00 68.45	8
	ATOM	7138	C	SER E	70		72.177	59.585	5.806	1.00 72.84	6
	ATOM	7139	0	SER E	70		73.254	59.212	6.304	1.00 73.59	8
	ATOM	7140	И	PRO E	71		71.065	59.789	6.550	1.00 71.65	7
15	ATOM	7141	CD	PRO E	71		69.793	60.434	6.160	1.00 70.63	6
15	ATOM	7142	CA	PRO E	71		71.091	59.521	7.989	1.00 69.54	6
	ATOM	7143	CB	PRO E	71		69.627	59.649	8.376	1.00 69.50	6
	ATOM	7144	CG	PRO E	71		69.172	60.783	7.505	1.00 69.75	6
	ATOM	7145	C	PRO E	71		71.611	58.104	8.128	1.00 67.45	6
20	ATOM	7146	Õ	PRO E	71		71.371	57.288	7.249	1.00 67.47	8
20	ATOM	7147	N	ASP E	72		72.332	57.813	9.202	1.00 65.90	7
	ATOM	7148	CA	ASP E	72		72.888	56.480	9.401	1.00 65.38	б
	ATOM	7149	СВ	ASP E	72		74.336	56.595	9.864	1.00 66.99	6
	MOTA	7150	CG	ASP E	72		74.623	57.933	10.513	1.00 69.68	6
25	ATOM	7151		ASP E	72		75.809	58.349	10.511	1.00 72.85	8
	ATOM	7152		ASP E	72		73.659	58.564	11.022	1.00 69.14	8
	ATOM	7153	С	ASP E	72		72.078	55.656	10.387	1.00 64.69	6
	ATOM	7154	Ō	ASP E	72		72.273	54.438	10.492	1.00 62.72	8
	ATOM	7155	N	GLN E	73		71.194	56.334	11.122	1.00 63.38	7
30	ATOM	7156	CA	GLN E	73		70.291	55.692	12.073	1.00 62.59	6
	ATOM	7157	CB	GLN E	73		70.703	55.968	13.502	1.00 63.56	6
	ATOM	7158	CG	GLN E	73		71.812	55.147	14.064	1.00 66.36	6
	ATOM	7159	CD	GLN E	73		72.073	55.601	15.478	1.00 69.74	6
	MOTA	7160	OE1	GLN E	73		72.311	56.794	15.711	1.00 71.52	8
35	ATOM	7161	NE2	GLN E	73		72.005	54.676	16.437	1.00 70.16	7
	MOTA	7162	С	GLN E	73		68.850	56.189	11.932	1.00 60.94	6
	MOTA	7163	0	GLN E	73		68.599	57.336	11.548	1.00 60.74	. 8
	MOTA	7164	N	VAL E	74		67.910	55.318	12.281	1.00 57.54	7
	MOTA	7165	CA	VAL E	74		66.495	55.652	12.254	1.00 54.00	6
40	MOTA	7166	CB	VAL E			65.857	55.296	10.901	1.00 52.88	6
	MOTA	7167		VAL E			66.391	56.201	9.814	1.00 52.07	6
	MOTA	7168	CG2	VAL E			66.151	53.846	10.564	1.00 53.11 1.00 51.46	6 6
	MOTA	7169	С	VAL E			65.816				8
	MOTA	7170	0	VAL E			66.355	53.838	13.804	1.00 51.44 1.00 48.05	7
45	MOTA	7171		SER E			64.649	55.299	13.789	1.00 45.32	6.
	MOTA	7172		SER E			63.893	54.592	14.812	1.00 43.32	6
	MOTA	7173		SER E			63.222	55.583	15.761	1.00 42.99	8
	MOTA	7174		SER E			64.122	56.022	16.763 14.123		6
	MOTA	7175		SER E			62.846	53.727	13.431	1.00 45.94	8
50	MOTA	7176		SER E			61.959	54.228	14.325	1.00 44.89	7
	ATOM	7177		VAL I			62.953		13.706		6
	MOTA	7178		VAL			62.052		12.943		6
	MOTA	7179		VAL I			62.857		12.296		6
	MOTA	7180		1 VAL E			61.930		11.907		6
55	ATOM	7181		2 VAL I			63.734		14.718		6
	ATOM	7182		VAL I			61.169 61.641		15.772		8
	ATOM	7183		VAL I			59.868		14.418		7
	ATOM	7184		PRO I			59.085		13.344		6
60	ATOM	7185					58.987		15.360		6
60	MOTA	7186					57.619		14.719		6
	ATOM	7187	7 CB	FAU.	_ //		٠,٠٠٠				

	WO 01/5	8951				٠				PC7	T/ <b>EP</b> 01/01	457
							-190				44 05	_
	MOTA	7188		PRO E			57.736	51.362	13.981	1.00		6 6
	MOTA	7189		PRO E			59.407 59.766	48.464 47.848	15.456 14.457	1.00		8
	ATOM	7190		PRO E			59.766	47.848	16.665	1.00		7
_	ATOM	7191		ILE E			59.729	46.550	16.938	1.00		6
5	MOTA	7192 7193	CA CB	ILE E			59.440	46.235	18.408		41.90	6
	MOTA MOTA	7193		ILE E			59.421	44.753	18.667	1.00	44.69	6
	ATOM	7195		ILE E			60.512	46.887	19.259	1.00	45.61	6
	ATOM	7196		ILE E			61.904	46.569	18.783		45.82	6
10	MOTA	7197	С	ILE E		3	59.002	45.562	16.048		39.58	6
	ATOM	7198	0	ILE E	3 7	3	59.556	44.550	15.645		39.79	8
	MOTA	7199	N	SER F			57.755	45.870	15.729		41.50	7
	MOTA	7200	CA	SER I			56.932	45.011	14.891		41.99 40.86	6 6
	MOTA	7201	CB	SER I			55.497	45.502	14.931 14.633		44.60	8
15	MOTA	7202	OG	SER I			55.441 57.370	46.876 44.887	13.441		43.24	6
	ATOM	7203	C	SER I			56.883	44.020	12.730		43.62	8
	MOTA MOTA	7204 7205	O	SER I			58.278	45.750	12.996		44.61	7
	ATOM	7205	CA	SER I			58.751	45.713	11.619		44.15	6
20	ATOM	7207	CB	SER I			58.841	47.133	11.062		43.26	6
	ATOM	7208	OG	SER			57.568	47.744	11.017		47.92	8
•	ATOM	7209	С	SER I	E 8	0	60.110	45.033	11.482		45.19	6
	ATOM	7210	0	SER		0	60.661	44.963	10.387		46.20	8
	ATOM	7211	N	LEU :			60.645	44.533	12.589		42.25	7
25	MOTA	7212	CA	LEU			61.949	43.891	12.577		42.76	6 6
	MOTA	7213	CB	LEU		1	62.950	44.702	13.400		41.44 39.51	6
	MOTA	7214	CG	LEU		1	63.144	46.190 46.826	13.150 14.314		38.48	6
	ATOM	7215		LEU LEU		1 1	63.861 63.908	46.367	11.891		43.00	6
30	ATOM ATOM	7216 7217	CDZ	LEU		1	61.846	42.530	13.216		42.93	6
30	ATOM	7217	0	LEU		1	60.845	42.221	13.865		47.16	8
	ATOM	7219	N	TRP		2	62.880	41.715	13.028	1.00	39.63	7
	ATOM	7220	CA	TRP		2	62.925	40.412	13.657		38.60	6
	ATOM	7221	CB	TRP		2	63.872	39.465	12.941		37.23	6
35	MOTA	7222	CG	TRP	E 8	2	64.186	38.241	13.753		39.34	6
	MOTA	7223	CD2			2	65.272	38.087	14.678		41.49	6
	ATOM	7224	CE2			2	65.142	36.811	15.266		40.40 41.39	6 6
	MOTA	7225	CE3			2	66.344	38.909 37.086	15.071 13.814		37.83	6
40	ATOM	7226		TRP		12 12	63.469 64.032	36.222	14.719		.40.75	7
40	MOTA	7227		TRP		32	66.044	36.335	16.228		39.91	6
	ATOM ATOM	7228 7229	CZ3			32	67.237	38,436	16.025		38.98	6
	ATOM	7230		TRP		32	67.080	37.161	16.591		40.84	. 6
	ATOM	7231	C	TRP		32	63.513	40.766	14.999		38.10	6
45	ATOM	7232	ō	TRP		32	64.356	41.636	15.086		39.18	8
	ATOM	7233	N	VAL	E 8	33	63.068	40.104	16.049		39.36	7
	ATOM	7234	CA	VAL		33	63.578	40.395	17.367		38.27	6
	ATOM	7235	CB	VAL		33	62.562	41.277	18.141		39.12	6
	ATOM	7236		VAL		33	62.919	41.352	19.596		43.60	6 6
50	ATOM	7237		VAL		33	62.557	42.678	17.565 18.089		37.11	6
	MOTA	7238		VAL		33	63.853 63.154	39.081 38.098	17.896		39.80	8
	ATOM	7239		VAL PRO		83 84	64.909	39.039	18.899		35.89	7
	MOTA	7240		PRO		84 .	65.921	40.088	19.075		38.94	6
55	MOTA MOTA	7241 7242		PRO		84	65.276	37.842	19.651	1.00	35.46	6
50	ATOM	7242		PRO		84	66.485	38.306	20.456	1.00	36.52	6
	ATOM	7244		PRO		84	67.087		19.600		37.91	6
	ATOM	7245		PRO		84	64.134	37.398			36.04	6
	MOTA	7246		PRO		84	63.541		21.246		34.75	8
60	MOTA	7247	N	ASP		85	63.839				33.87	7
	ATOM	7248	CA	ASP	E	85	62.771	35.595	21.400	1.00	35.26	6

•	WO 01/5	8951								PCT/EP01/	01457
							-191				
	ATOM	7249	СВ	ASP E	2	85	62.150	34.350	20.779	1.00 37.18	6
	ATOM	7250		ASP I		85	63.150	33.259	20.556	1.00 40.21	6
	ATOM	7251		ASP E	2	85	64.268	33.583	20.129	1.00 41.52	. 8
	ATOM	7252	OD2	ASP F	S	85	62.828	32.079	20.789	1.00 38.39	8
5	ATOM	7253	С	ASP I	<b>Ξ</b>	85	63.277	35.290	22.794	1.00 36.88	6
	MOTA	7254		ASP I		85	63.139	34.174	23.287	1.00 37.96	8
	MOTA	7255		LEU 1		86	63.848	36.307	23.427	1.00 34.95	7 6
	ATOM	7256		LEU I		86	64.387		24.769	1.00 36.75 1.00 36.06	
4.0	ATOM	7257	CB	LEU I		86	65.211	37.414 37.646	25.116 24.221	1.00 34.31	
10	MOTA	7258	CG	LEU !		86	66.410	38.893	24.221	1.00 32.72	
	ATOM	7259		LEU !		86 86	67.131 67.300	36.446	24.033	1.00 35.49	
	ATOM	7260		LEU !		86 86	63.317	36.021	25.816	1.00 37.61	
	MOTA	7261	C 0	LEU :		86	62.226	36.557	25.694	1.00 41.91	
15	ATOM	7262 7263 ·	Ŋ	ALA		87	63.652	35.293	26.865	1.00 38.39	
15	ATOM ATOM	7264	CA	ALA		87	62.727	35.060	27.949	1.00 39.76	
	ATOM	7265	CB	ALA		87	61.950	33,766	27.692	1.00 37.37	6
	MOTA	7266	C	ALA		87	63.510	34.959	29.255	1.00 41.61	
	ATOM	7267	Ö	ALA		87	64.583	34.372	29.288	1.00 42.91	
20	ATOM	7268	N	ALA		88	62.989	35.550	30.323	1.00 41.72	
	ATOM	7269	CA	ALA	E	88	63.639	35.460	31.624	1.00 40.16	
	MOTA	7270	CB	ALA	E	88	63.259	36.638	32.480	1.00 38.02	
	MOTA	7271	C	ALA		88	63.154	34.168	32.261	1.00 41.60	
	MOTA	7272	0	ALA		88	62.028	34.089	32.740	1.00 43.75	
25	MOTA	7273	N	TYR		89	64.008	33.152	32.245 32.793	1.00 43.12	
	ATOM	7274	CA	TYR		89	63.691	31.832 31.010	32.793	1.00 47.55	_
	MOTA	7275	CB	TYR		89	64.970 65.633	30.711	31.573	1.00 53.63	
	MOTA	7276 7277	CG	TYR TYR		89 89	66.903	30.711	31.521	1.00 54.69	
30	MOTA MOTA	7277		TYR		89	67.519	29.831	30.311	1.00 56.44	1 6
00	ATOM	7279		TYR		89	64.995	31.006	30.368	1.00 56.03	
	ATOM	7280	CE2			89	65.599	30.720	29.147	1.00 58.8	
	ATOM	7281	CZ	TYR	E	89	66.860	30.131	29.125	1.00 58.83	
	MOTA	7282	OH	TYR		89	67.437	29.821	27.908	1.00 64.1	
35	MOTA	7283	С	TYR		89	62.959	31.792	34.138	1.00 44.63	
	MOTA	7284	0	TYR		89	62.113	30.920	34.362	1.00 43.1° 1.00 43.5°	
	ATOM	7285	N	ASN		90	63.275	32.723	35.036 36.338	1.00 43.9	
	MOTA	7286	CA	ASN		90	62.621 63.658	32.729 32.682	37.469	1.00 41.3	
40	MOTA	7287	CB	ASN		90 90	64.654	33.809	37.401	1.00 40.9	
40	ATOM	7288	CG	ASN ASN		90	65.197	34.116	36.341	1.00 40.1	
	MOTA MOTA	7289 7290		ASN		90	64.914	34.425	38.542	1.00 42.1	
	MOTA	7291	C	ASN		90	61.668	33.894	36.538	1.00 45.2	2 6
	MOTA	7292	ō	ASN		90	61.397	34.296	37.668	1.00 45.1	
45	ATOM	7293	N	ALA		91	61.170	34.437	35.432	1.00 46.1	
	MOTA	7294	CA	ALA		91	60.207	35.526	35.482	1.00 44.2	
	ATOM	7295	CB	ALA	E	91	59.974	36.095	34.110	1.00 43.1	
	MOTA	7296	С	ALA		91	58.937	34.881	36.006	1.00 45.1	
	MOTA	7297	0	ALA		91	58.543	33.800	35.577	1.00 43.2 1.00 46.1	
50	MOTA	7298		ILE		92	58.306	35.569	36.940	1.00 45.1	
	MOTA	7299		ILE		92	57.111	35.100 35.365	37.611 39.123	1.00 49.0	
	MOTA	7300		ILE		92 92 ·	57.301 ·56.517	36.598	39.568	1.00 53.3	
	MOTA	7301		2 ILE 1 ILE		92	56.883	34.165	39.929	1.00 50.5	
55	MOTA	7302 7303		1 ILE		92	56.902	34.482			
J	MOTA MOTA	7303		ILE		92	55.863	35.805		1.00 43.2	7 6
	MOTA	7305		ILE		92	54.745	35:458		1.00 40.9	7 8
	MOTA	7306		SER		93	56.078	36.806	36.216	1.00 42.5	
	MOTA	7307		SER	E		55.001	37.573			
60	MOTA	7308	CB	SER	E	93	54.765				
	MOTA	7309	OG	SER	Ε	93	55.849	39.756	36.170	1.00 40.4	2 8

	WO 01/5	8951							PCT/EP01/01	<b>4</b> 57
						-192				
	ATOM	7310	С	SER E	93	55.497	37.925	34.214	1.00 41.98	6
	ATOM	7311		SER E	93	56.686	37.781	33.932	1.00 43.61	8
	ATOM	7312	N	LYS E	94	54.617	38.380	33.333	1.00 41.47	7
	ATOM	7313	CA	LYS E	94	55.109	38.738	32.018	1.00 44.98	6
5	MOTA	7314	СВ	LYS E	94	54.037	38.561	30.942	1.00 44.95	6
_	ATOM	7315	CG	LYS E	94	52.663	39.071	31.264	1.00 48.24	6
	MOTA	7316	CD	LYS E	94	51.659	38.499	30.255	1.00 50.47	6
	MOTA	7317	CE	LYS E	94	52.173	38.628	28.822	1.00 53.56	6
	MOTA	7318	NZ	LYS E	94	51.218	38.125	27.795	1.00 54.79	7
10	MOTA	7319		LYS E	94	55.675	40.151	32.031	1.00 45.16	6
	MOTA	7320	0	LYS E	94	55.386	40.939	32.933	1.00 46.22	8 7
	MOTA	7321	N	PRO E	95	56.514	40.481	31.038 29.926	1.00 43.95 1.00 42.19	6
	MOTA	7322	CD	PRO E	95 25	56 973	39.633 41.802	30.957	1.00 42.13	6
15	MOTA	7323	CA	PRO E	95 95	57.131 58.076	41.671	29.768	1.00 42.81	6
15	MOTA	7324 7325	CB CG	PRO E	95 95	58.306	40.216	29.636	1.00 42.27	6
	ATOM	7325	C	PRO E	95	56.162	42.939	30.761	1.00 42.70	6
	ATOM ATOM	7327	0	PRO E	95	55.320	42.899	29.870	1.00 46.65	8
	MOTA	7328	N	GLU E	96	56.269	43.952	31.601	1.00 40.32	7
20	ATOM	7329	CA	GLU E		55.424	45.115	31.446	1.00 41.45	6
	ATOM	7330	CB	GLU E	96	54.910	45.635	32.797	1.00 42.90	6
	MOTA	7331	CG	GLU E	96	53.911	46.797	32.674	1.00 47.98	6
	MOTA	7332	CD	GLU E		53.396	47.308	34.024	1.00 50.94	6
	ATOM	7333	-	GLU E		53.482	46.539	35.005	1.00 53.57	8
25	MOTA	7334		GLU E		52.894	48.462	34.102	1.00 47.79	8 6
	MOTA	7335	C	GLU E		56.372 57.143	46.123 46.762	30.830	1.00 40.44	8
	MOTA	7336	0	GLU E		56.348	46.702	29.506	1.00 36.63	7
	ATOM ATOM	7337 7338	N CA	VAL E	_	57.200	47,165	28.800	1.00 34.15	6
30	MOTA	7339	CB	VAL E	-	57.230	46.850	27.311	1.00 31.33	6
-	MOTA	7340		VAL E		58.136	47.814	26.596	1.00 31.45	6
	MOTA	7341	CG2	VAL E	97	57.708	45.444	27.113	1.00 28.98	6
	MOTA	7342	C	VAL E		56.665	48.576	29.041	1.00 35.79	6
	ATOM	7343	0	VAL E		55.558	48.932	28.636	1.00 35.88	8
35	MOTA	7344	N	LEU E		57.474	49.378	29.714	1.00 35.63	7 6
	MOTA	7345	CA	LEU I		57.091	50.725	30.086 31.395	1.00 36.41 1.00 34.14	6
	MOTA	7346	CB	LEU E		57.787 57.676	51.098 50.176	32.598	1.00 33.56	6
	MOTA	7347 7348	CG CD1	LEU I		58.694	50.570	33.602	1.00 31.56	6
40	MOTA MOTA	7349	CD2			56.306	50.248	33.190	1.00 33.37	6
	MOTA	7350	C	LEU I		57.400	51.793	29.058	1.00 36.97	6
	ATOM	7351	Ö	LEU I		56.969	52.936	29.203	1.00 38.13	8
	MOTA	7352	N	THR I		58.133	51.426	28.018	1.00 35.68	7
	ATOM	7353	CA	THR I		58.533	52.391	27.011	1.00 34.41	6
45	MOTA	7354	CB	THR I		60.067	52.547	27.032	1.00 35.73	6
	MOTA	7355		THR I		60.683	51.265	26.850	1.00 39.59	8
	MOTA	7356				60.517	53.122	28.355	1.00 34.05 1.00 33.50	6 6
	ATOM	7357	C	THR		58.098 57.696	52.084 50.969	25.589 25.283	1.00 33.37	8
50	MOTA	7358	0	THR I	Ξ 99 Ξ <b>1</b> 00	58.155	53.093	24.701	1.00 34.01	7
50	MOTA MOTA	7359 7360			E 100	58.424	54.514	24.975	1.00 36.06	6
	ATOM	7361			E 100	57.777	52.919	23,302	1.00 33.45	6
	ATOM	7362			E 100	58.227	54.223	22.669	1.00 31.60	6
	ATOM	7363			E 100	57.906	55.190	23.725	1.00 32.57	6
55	MOTA	7364			E 100	58.529	51.719	22.769	1.00 35.44	6
	MOTA	7365			E 100	59.713	51.546	23.041	1.00 35.44	8
	MOTA	7366			E 101	57.844	50.868	22.029	1.00 37.12	7
	ATOM	7367			E 101	58.514 57 551	49.701	21.516 21.476	1.00 38.35 1.00 39.07	6 6
60	ATOM	7368			E 101 E 101	57.551 57.398	48.532 47.921	22.845		6
υψ	ATOM ATOM	7369 7370			E 101	56.194	47.037	22.948		6

	WO 01/5	8951								PCT/EI	201/01	457
							-193					
	MOTA	7371	OE1	GLN E	101		56.055	46.068	22.194	1.00 50.	74	8
	MOTA	7372		GLN E			55.298	47.359	23.885	1.00 48.		7
	ATOM	7373		GLN E			59.146	49.950	20.181	1.00 37.		6
•	MOTA	7374		GLN E			58.749	49.374	19.177	1.00 36		8
5	ATOM	7375		LEU E			60.153	50.825	20.213	1.00 39		7 6
	MOTA	7376		LEU E		•	60.936	51.230	19.046	1.00 38		6
	MOTA	7377		LEU E			60.911	52.749	18.880	1.00 36		6
	MOTA	7378		LEU E			59.545	53.416 54.906	18.766 18.615	1.00 37		6
40	MOTA	7379		LEU E			59.712 58.809	52.853	17.571	1.00 37		6
10	MOTA	7380	CD2	LEU E			62.374	50.791	19.207	1.00 37		6
	MOTA MOTA	7381 7382	0	LEU E			62.909	50.784	20.312	1.00 40		8
	ATOM	7382	N	ALA E			62.995	50.408	18.102	1.00 37	.36	7
	ATOM	7384	CA	ALA E			64.395	50.007	18.127	1.00 38	.78	6
15	ATOM	7385	СВ	ALA E			64.577	48.634	17.504	1.00 37		6
	ATOM	7386	С	ALA E	103		65.193	51.039	17.351	1.00 38		6
	MOTA	7387	0	ALA E	103		64.645	51.890	16.666	1.00 38		8
	MOTA	7388	N	ARG E			66.500	50.969	17.469	1.00 40		7
	MOTA	7389	CA	ARG E			67.344	51.911	16.770	1.00 44		6
20	MOTA	7390	СВ	ARG E			68.258	52.612	17.771	1.00 44 1.00 45		6 6
	MOTA	7391	CG	ARG E			68.873	53.873	17.251 16.983	1.00 43		6
	MOTA	7392	CD	ARG E			67.868 68.570	54.956 56.118	16.456	1.00 45		7
	MOTA	7393	NE	ARG E			68.008	57.289	16.175	1.00 46		.6
25	MOTA	7394	CZ	ARG E			66.711	57.493	16.365	1.00 47		7
25	ATOM ATOM	7395 7396		ARG E			68.760	58.266	15.698	1.00 49		7
	MOTA	7397	C	ARG E			68.142	51.099	15.763	1.00 46		6
	ATOM	7398	Ö	ARG E			68.775	50.105	16.119	1.00 47	.46	8
	MOTA	7399	N	VAL I			68.081	51.492	14.497	1.00 48		7
30	MOTA	7400	CA	VAL E			68.808	50.761	13.475	1.00 49		6
	MOTA	7401	CB	VAL E	105		67.869	50.244	12.388	1.00 49		6
	MOTA	7402	CG1	VAL I	105		68.643	49.361	11.431	1.00 49		6
	MOTA	7403	CG2	VAL I			66.731	49.478	13.010	1.00 49		6
	ATOM	7404	C	VAL I			69.883	51.601	12.805	1.00 51 1.00 49		6 8
35	ATOM	7405	0	VAL			69.606	52.684	12.272 12.834	1.00 43		7
	MOTA	7406	N	VAL I			71.109 72.265	51.077 51.738	12.232	1.00 55		6
	MOTA	7407	CA	VAL			73.537	51.738	13.009	1.00 54		6
	MOTA	7408 7409	CB CC1	VAL I			74.666	52.300	12.539	1.00 55		6
40	ATOM ATOM	7410		VAL :			73.283	51.577	14.507	1.00 57		6
40	ATOM	7410	C		E 106		72.428	51.253	10.795	1.00 55		6
	ATOM	7412	Ö		E 106		72.213	50.075	10.508	1.00 57		8
	MOTA	7413	N		E 107		72.812	52.153	9.897	1.00 55		7
	ATOM	7414	CA		E 107		72.972	51.812	8.486	1.00 55		6
45	MOTA	7415	CB		E 107		73.610	52.984	7.740	1.00 55		6
	ATOM	7416	OG		E 107		74.708	53.503	8.470	1.00 58		8
	MOTA	7417	С		E 107		73.738	50.530	8.175	1.00 54		б
	MOTA	7418	0		E 107		73.578	49.966	7.096	1.00 52 1.00 53		8 7
	MOTA	7419	N		E 108		74.558	50.062	9.105	1.00 5		6
50	MOTA	7420			E 108		75.324	48.847	8.862 9.548	1.00 5		6
	MOTA	7421			E 108		76.691	48.938 48.911	11.055	1.00 6		6
	ATOM	7422			E 108		76.597 75.653	49.522	11.599	1.00 6		8
	MOTA	7423		L ASP 2 ASP			77.479	48.296	11.694	1.00 6		8
55	ATOM	7424 7425			E 108		74.612		9.288	1.00 5		6
55	MOTA MOTA	7425			E 108		75.213		9.278	1.00 5		8
	MOTA	7427			E 109		73.337		9.662	1.00 6		7
	MOTA	7428			E 109		72.559		10.072	1.00 6		6
	ATOM	7429			E 109		72.581		11.563	1.00 6		· 6
60	ATOM	7430			E 109		72.031	45.211	12.011			8
- •	MOTA	7431			E 110		73.215	47.100	12.342	1.00 6	1.69	7

PCT/EP01/01457

	WO 01/5	וכעש						PC1/EPU1/U.	1457
					-194				
	3 5034	7420	C1	GLU E 110	73.283	46.899	13.787	1,00 61.54	6
	MOTA	7432		GLU E 110	74.432	47.720	14.391	1.00 64.16	6
	MOTA	7433			74.946	47.231	15.755	1.00 67.88	6
	MOTA	7434		GLU E 110	75.559	45.828	15.684	1.00 72.22	6
_	MOTA	7435		GLU E 110 GLU E 110	75.936	45.401	14.554	1.00 72.61	8
5	MOTA	7436			75.536 75.676	45.165	16.758	1.00 70.57	. 8
	MOTA	7437		GLU E 110	71.948	47.368	14.347	1.00 60.20	6
	MOTA	7438		GLU E 110	71.421	48.418	13.949	1.00 59.08	8
	MOTA	7439		GLU E 110	71.421	46.581	15.266	1.00 57.63	7
10	MOTA	7440		VAL E 111	70.116	46.893	15.885	1.00 54.53	6
10	MOTA	7441		VAL E 111	69.065	45.797	15.557	1.00 53.43	6
	MOTA	7442		VAL E 111	67.728	46.159	16.178	1.00 53.30	6
	MOTA	7443		VAL E 111	68.932	45.631	14.053	1.00 52.07	6
	ATOM	7444		VAL E 111	70.231	47.017	17.406	1.00 52.96	6
4.5	MOTA	7445		VAL E 111	70.231	46.170	18.066	1.00 52.11	8
15	MOTA	7446	0	VAL E 111	69.641	48.070	17.961	1.00 50.09	7
	ATOM	7447	N	LEU E 112	69.687	48.261	19.399	1.00 50.92	6
	ATOM	7448	CA	LEU E 112	70.546	49.468	19.770	1.00 55.28	6
	MOTA	7449	CB	LEU E 112		49.466	18.992	1.00 58.58	6
	MOTA	7450	CG	LEU E 112	71.820 72.649	49.640	18.629	1.00 59.41	6
20	MOTA	7451		LEU E 112		50.603	17.742	1.00 58.46	6
	MOTA	7452		LEU E 112	71.428	48.485	19.930	1.00 50.61	6
	MOTA	7453	C	LEU E 112	68.286	49.437		1.00 50.59	8
	MOTA	7454	Ο.	LEU E 112	67.628	47.597	20.816	1.00 49.12	7
	MOTA	7455	N	TYR E 113	67.835		21.420	1.00 46.39	6
25	MOTA	7456	CA	TYR E 113	66.514	47.690 46.500	21.420	1.00 45.58	6
	MOTA	7457	CB	TYR E 113	65.635	46.491	21.610	1.00 44.58	6
	MOTA	7458	CG	TYR E 113	64.235		21.655	1.00 45.06	6
	MOTA	7459		TYR E 113	63.453	47.650	22.177	1.00 44.35	6
	MOTA	7460	CE1		62.162	47.632	22.177	1.00 43.68	6
30	MOTA	7461	CD2		63.684	45.318	22.105	1.00 45.23	6
	MOTA	7462	CE2	TYR E 113	62.395	45.287		1.00 45.23	6
	MOTA	7463	CZ	TYR E 113	61.633	46.444	22.663	1.00 46.01	8
	MOTA	7464	OH	TYR E 113	60.346	46.399	23.183	1.00 46.41	6
	MOTA	7465	С	TYR E 113	66.721	47.679	22.915	1.00 46.41	8
35	MOTA	7466	0	TYR E 113	67.194	46.697	23.463	1.00 46.43	7
	ATOM	7467	N	MET E 114	66.363	48.774	23.572	1.00 48.35	6
	MOTA	7468	CA	MET E 114	66.539	48.880	25.011	1.00 48.33	6
	MOTA	7469	CB	MET E 114	67.635	49.889	25.315	1.00 56.27	6
	ATOM	7470	CG	MET E 114	68.053	49.906	26.737	1.00 55.32	16
40	MOTA	7471	SD	MET E 114	68.981	51.368	27.017 26.425	1.00 63.32	6
	MOTA	7472	CE	MET E 114	70.586	50.862			6
	MOTA	7473	С	MET E 114	65.255			1.00 50.19	8
	MOTA	7474	Ò	MET E 114	65.095	50.494	26.036	1.00 30.19	7
	ATOM	7475	N	PRO E 115	64.325	48.383	25.920	1.00 47.93	6
45	MOTA	7476	CD	PRO E 115	64.341	46.978	25.467	1.00 46.04	6
	MOTA	7477	CA	PRO E 115	63.056	48.702	26.572	1.00 46.59	6
	MOTA	7478	CB	PRO E 115	62.150	47.590	26.077 26.083	1.00 45.01	6
	MOTA	7479		PRO E 115	63.080	46.411		1.00 44.33	6
	MOTA	7480		PRO E 115	63.184	48.685	28.080	1.00 44.22	8
50	MOTA	7481		PRO E 115	63.997	47.940	28.619		7
	MOTA	7482		SER E 116	62.397	49.510	28.761 30.217		6
	MOTA	7483		SER E 116	62.428	49.514			6
	MOTA	7484		SER E 116	62.113	50.884	30.773		8
	MOTA	7485		SER E 116	62.191	50.841	32.181		6
55	ATOM	7486		SER E 116	61.344	48.533	30.643 30.246		8
	MOTA	7487		SER E 116	60.196	48.672			7
	ATOM	7488		ILE E 117	61.704	47.544	31.449 31.851		
	MOTA	7489		ILE E 117	60.751	46.534	31.851		
^^	MOTA	7490		ILE E 117	61.182	45.152			
60	MOTA	7491		2 ILE E 117	60.251		31.792 29.787		
	MOTA	7492	CG:	L ILE E 117	61.207	45.173	23.101	1.00 30.02	3

	WO 01/5	8951							PCT/E	P01/01	457
						-195					
	MOTA	7493	CD1	ILE E	3 117	61.883	43.985	29.185	1.00 35		6
	MOTA	7494	C	ILE E		60.561	46.387	33.349	1.00 43		6
	MOTA	7495	0	ILE F		61.525	46.400	34.116	1.00 44		8
_	MOTA	7496	N	ARG I		59.305	46.266	33.768	1.00 43		7 6
5	MOTA	7497	CA	ARG I		59.014 57.007	46.009 46.897	35.170 35.710	1.00 42		6
	ATOM	7498	CB	ARG I		57.907 57.537	46.484	37.113	1.00 39		6
	MOTA MOTA	7499 7500	CG CD		E 118	56.671	47.482	37.113	1.00 40		6
	ATOM	7501	NE		E 118	56.321	46.985	39.155	1.00 40		7
10	ATOM	7501	CZ		E 118	55.762	47.717	40.108	1.00 38		6
	ATOM	7503		ARG		55.485	48.991	39.899	1.00 43	1.07	7
	ATOM	7504		ARG		55.486	47.175	41.273	1.00 3		7
	MOTA	7505	С		E 118	58.552	44.557	35.140	1.00 43		6
	ATOM	7506	0	ARG :	E 118	57.738	44.185	34.309	1.00 43		8
15	ATOM	7507	N		E 119	59.071	43.731	36.036	1.00 43		. 7
	MOTA	7508	CA		E 119	58.718	42.321	36.016	1.00 43		6
	MOTA	7509	CB		E 119	59.460	41.671	34.842	1.00 4		6
	MOTA	7510	CG		E 119	59.220	40.211	34.624	1.00 4		6 6
20	MOTA	7511	CD		E 119 E 119	59.795 60.829	39.749 40.227	33.304 32.879	1.00 4		8
20	MOTA MOTA	7512 7513	OE1 NE2		E 119	59.126	38.807	32.654	1.00 4		7
	ATOM	7513	C		E 119	59.085	41.658	37.337	1.00 4		6
	ATOM	7515	0		E 119	60.030	42.059	38.006	1.00 4		8
	ATOM	7516	N		E 120	58.326	40.649	37.724	1.00 4		7
25	ATOM	7517	CA		E 120	58.612	39.958	38.969	1.00 4	9.63	б
-	MOTA	7518	CB		E 120	57.327	39.657	39.722	1.00 5		6
	MOTA	7519	CG		E 120	56.514	40.879	40.037	1.00 5		6
	MOTA	7520	CD		E 120	55.730	40.641	41.301	1.00 6		6
	MOTA	7521	NE		E 120	56.517	40.896	42.518	1.00 6		7
30	MOTA	7522	CZ		E 120	56.467	40.125	43.606	1.00 6 1.00 6		6 7
	ATOM	7523			E 120	55.687 57.150	39.045 40.459	43.617 44.702	1.00 6		7
	MOTA	7524	NH2		E 120 E 120	59.365	38.662	38,724	1.00 4		6
	ATOM ATOM	7525 7526	C O		E 120	59.187	38.013	37.692	1.00 4		8
35	MOTA	7527	N		E 121	60.210	38.295	39.683	1.00 4		7
00	ATOM	7528	CA		E 121	60.996	37.085	39.563	1.00 4	6.24	6
	ATOM	7529	CB		E 121	62.453	37.408	.39.224	1.00 4	2.79	б
	MOTA	7530	CG		E 121	62.620	38.238	38.001	1.00 4		6
	MOTA	7531			E 121	62.431	39.605	38.052	1.00 4		6
40	MOTA	7532			E 121	62.945	37.651	36.793	1.00 4	_	6
	MOTA	7533			E 121	62.559	40.372	36.924	1.00 4		6
	MOTA	7534			E 121	63.074	38.406	35.667	1.00 3		6
	MOTA	7535	CZ		E 121	62.881	39.770 36.243	35.725 40.812	1.00 4		6 6
45	MOTA	7536	C		E 121	60.991 60.663	36.708	41.902	1.00 4		8
40	MOTA	7537	N		E 121 E 122	61.381	34.987	40.619	1.00 5		7
	MOTA MOTA	7538 7539	CA		E 122	61.509	34.019	41.691	1.00 5		6
	ATOM	7540	СВ		E 122	60.846	32.701	41.302	1.00 5		6
	MOTA	7541	OG		E 122	60.993	31.753	42.338	1.00 5	4.83	8
50	ATOM	7542	C.		E 122	63.007	33.817	41.838	1.00 5	1.59	6
	MOTA	7543	0	SER	E 122	63.648	33.274	40.947	1.00 5		8
	MOTA	7544	N		E 123	63.566	34.282	42.946	1.00 5		7
	ATOM	7545	CA		E 123	65.000	34.155	43.186	1.00 5		6
	MOTA	7546	C		E 123	65.301	34.247	44.680	1.00 5		6
55	ATOM	7547	0.		E 123	64.390	34.401	45.501	1.00 5		8 6
	MOTA	7548	CB		E 123	65.757 65.215	35.249 36.927	42.425 42.881	1.00 5		16
	MOTA	7549	SG		E 123 E 124	66.581	34.151	45.033	1.00 6		7
	MOTA	7550 7551	N CA		E 124		34.215	46.437	1.00 6		6
60	MOTA MOTA	7551 7552	CB	ASP	E 124	68.406	33.650	46.620	1.00		6
33	MOTA	7553	CG		E 124	68.605	33.024	47.992	1.00 6		6

	WO 01/58	8951							PCT	/ <b>EP</b> 01/01	457
						-196					
	ATOM	7554	OD1	ASP I	E 124	67.970	33.502	48.967	1.00	63.75	8
	ATOM	7555			E 124	69.396	32.058	48.094	1.00	65.17	8
	MOTA	7556			E 124	66.953	35.636	47.007	1.00		6
	MOTA	7557	0	ASP :	E 124	67.748	36.495	46.630	1.00		8
5	MOTA	7558	N	VAL :	E 125	66.031	35.857	47.936	1.00		7
	MOTA	7559	CA	VAL	E 125	65.869	37.152	48.586	1.00		6
	MOTA	7560	_		E 125	64.370	37.506	48.710	1.00		6
	MOTA	7561			E 125	64.195	38.794	49.466		58.52	6
	MOTA	7562			E 125	63.751	37.608	47.331		59.91	- 6
10	MOTA	7563			E 125	66.501	37.157	49.987		64.88	б
	MOTA	7564	0		E 125	66.768	38.214	50.551		66.59	8 7
	MOTA	7565	N		E 126	66.745	35.975	50.544		64.96	6
	MOTA	7566	CA		E 126	67.335	35.870	51.874		64.47 62.82	6
4-	MOTA	7567	CB		E 126	67.672	34.410	52.185 51.267		61.35	8
15	MOTA	7568	OG		E 126	68.617	33.901	52.013		65.71	6
	ATOM	7569	C		E 126	68.588 69.494	36.729 36.690	51.165		65.59	8
	ATOM	7570	0		E 126 E 127	68.632	37.519	53.082		66.30	7
	ATOM ATOM	7571 7572	N CA		E 127	69.788	38.369	53.309		67.81	6
20	MOTA	7573	CA		E 127	69.595	39.800	52.848		69.06	6
20	ATOM	7574	0		E 127	70.471	40.633	53.037		69.45	8
	MOTA	7575	N		E 128	68.444	40.093	52.253	1.00	70.68	7
	ATOM	7576	CA		E 128	68.179	41.438	51.771	1.00	72.21	6
	ATOM	7577	CB		E 128	66.784	41.575	51.127	1.00	70.88	6
25	ATOM	7578			E 128	66.771	40.882	49.794	1.00	74.99	6
	MOTA	7579			E 128	65.722	40.993	52.039	1.00	69.09	6
	ATOM	7580	C		E 128	68.233	42.480	52.855	1.00	73.85	6.
	ATOM	7581	0	VAL	E 128	68.855	43.525	52.678		74.59	8
	MOTA	7582	N	ASP	E 129	67.579	42.197	53.977		75.59	7
30	MOTA	7583	CA		E 129	67.506	43.170	55.046		77.34	6
	MOTA	7584	CB		E 129	66.583	42.691	56.164		78.29	6
	ATOM	7585	CG		E 129	65.952	43.864	56.939		80.26	6
	MOTA	7586			E 129	64.733	43.805	57.257		82.07	8
0.5	MOTA	7587			E 129	66.674	44.848	57.231		78.55 78.37	8 6
35	MOTA	7588	C	_	E 129	68.825	43.625	55.628		78.49	8
	ATOM	7589	0		E 129	68.852	44.624 42.942	56.362 55.302		79.16	7
	MOTA	7590	N		E 130 E 130	69.925 71.201	43.391	55.847		80.17	6
	MOTA	7591 7592	CA CB		E 130	71.162	43.351	57.393		83.36	6
40	ATOM ATOM	7593	OG1		E 130	70.028	42.564	57.803		84.91	8
40	ATOM	7594	CG2		E 130	71.096	44.810	57.995		82.87	. 6
	ATOM	7595	C		E 130	72.505	42.731	55.445		78.82	6
	ATOM	7596	Ö		E 130	72.549	41.553	55.068		78.45	8
	ATOM	7597	N		E 131	73.564	43.537	55.572	1.00	78.85	7
45	ATOM	7598	CA		E 131	74.961	43.153	55.353	1.00	78.23	6
	MOTA	7599	СВ		E 131	75.292	41.900	56.187	1.00	80.76	6
	MOTA	7600	CG	GLU	E 131	75.507	42.176	57.686		82.62	6
	ATOM	76,01	CD		E 131	75.241	40.955	58.543		83.46	6
	MOTA	7602			E 131	75.740	3 <i>9.</i> 854	58.186		83.49	8
50	MOTA	7603	OE2		E 131	74.534	41.107	59.565		83.07	. 8
	ATOM	7604	С	-	E 131	75.434	42.931	53.943		77.11	6
	MOTA	7605	0		E 131	75.646	43.884	53.173		75.95	8
	ATOM	7606	N		E 132	75.658	41.652	53.650		76.20 75.57	7
EE	ATOM	7607	CA		E 132	76.107	41.200	52.352 52.501		75.40	6 6
55	ATOM	7608	CB		E 132	76.773	39.831 38.911	53.122		73.45	8
	MOTA	7609	OG C		E 132	75.896 74.858	41.115	51.462		74.79	6
	MOTA	7610	C		E 132	74.926	40.722	50.288		76.37	8
	MOTA MOTA	7611 7612	N O		E 133	73.719	41.484	52.048		72.67	7
60	ATOM	7612	CA		E 133	72.459	41.482	51.330		69.80	6
-	MOTA	7614	Ċ		E 133	72.127	40.179	50.631		67.70	6

	WO 01/5	8951							PCT/	<b>EP</b> 01/01	457
						-197					
	ATOM	7615	0	GLY E	: 133	72.686	39.128	50.934	1.00 6	7.31	8
	MOTA	7616		ALA E		71.205	40.256	49.681	1.00 6	6.03	7
	ATOM	7617		ALA E		70.799	39.081	48.931	1.00 6	4.43	6
	MOTA	7618	СВ	ALA E		69.275	38.990	48.879	1.00 6	4.83	6
5	MOTA	7619	С	ALA E	134	71.363	39.108	47.512	1.00 6		6
	MOTA	7620	0	ALA E	E 134	71.825	40.148	47.014	1.00 6		. 8
	MOTA	7621	N	THR E		71.339	37.944	46.875	1.00 6		7
	ATOM	7622	CA	THR I		71.813	37.817	45.515	1.00 6		6
40	MOTA	7623	CB	THR I		73.108	37.043	45.446	1.00 6		6
10	MOTA	7624		THR I		74.093	37.715	46.237	1.00 6		8 6
	MOTA	7625	CG2	THR I		73.590 70.741	36.970 37.102	44.012 44.718	1.00 6		6
	MOTA MOTA	7626 7627	C	THR I		70.522	35.886	44.839	1.00 5		8
	MOTA	7628	N	CYS I		70.049	37.901	43.919	1.00 5		7
15	ATOM	7629	CA	CYS I		68.975	37.422	43.083	1.00 5		6
	ATOM	7630	C		3 136	69.530	37.254	41.669	1.00 5		6
	ATOM	7631	Ö		3 136	69.990	38.220	41.054	1.00 5	4.61	8
	ATOM	7632	СВ	CYS I	≆ 136	67.843	38.442	43.129	1.00 5	55.65	6
	ATOM	7633	SG	CYS 1	<b>E</b> 136	66.510	38.178	41.946	1.00 5		16
20	ATOM	7634	N		<b>3</b> 137	69.517	36.016	41.180	1.00		7
	MOTA	7635	CA		<b>≅ 137</b>	70.025	35.717	39.853	1.00 5		6
	ATOM	7636	CB		E 137	70.861	34.437	39.871	1.00 5		6
	MOTA	7637	CG		E 137	72.068	34.513	40.774	1.00 6		6 6
OF	MOTA	7638	CD		E 137	72.482	33.125	41.241 42.500	1.00 (		7
25	MOTA	7639	NE		E 137	73.230 74.469	33.182 33.659	42.500	1.00		6
	MOTA MOTA	7640 7641	CZ	ARG	E 137	75.134	34.130	41.578	1.00		7
	ATOM	7642		ARG		75.042	33.674	43.832	1.00		7
	ATOM	7643	C		E 137	68.863	35.545	38.894	1.00 5		6
30	ATOM	7644	Ö		E 137	67.909	34.822	39.177	1.00 !		8
	ATOM	7645	N		E 138	68.970	36.215	37.754	1.00	54.63	7
	MOTA	7646	CA	ILE	E 138	67.966	36.175	36.716	1.00 !		6
	ATOM	7647	CB		E 138	67.432	37.587	36.468	1.00		6
	MOTA	7648	CG2		E 138	66.432	37.573	35.333	1.00		6
35	MOTA	7649	CG1		E 138	66.817	38.137	37.757	1.00		6
	MOTA	7650	CD1		E 138	66.476	39.606	37.681	1.00		6
	MOTA	7651	C		E 138	68.611	35.655	35.434	1.00 !		6 8
	ATOM	7652	0		E 138 E 139	69.557 68.105	36.261 34.542	34.933 34.901	1.00		7
40	ATOM ATOM	7653 7654	N CA		E 139	68.656	33.961	33.667	1.00		6
40	ATOM	7655	CB		E 139	68.877	32.455	33.822	1.00		6
	ATOM	7656	CG		E 139	69.732	32.075	35.013	1.00		6
	MOTA	7657	CD		E 139	70.150	30.612	34.967	1.00		6
	ATOM	7658	CE		E 139	71.183	30.363	33.869	1.00		6
45	MOTA	7659	NZ	LYS	E 139	71.624	28.928	33.787	1.00		7
	MOTA	7660	·C	LYS	E 139	67.738	34.187	32.480	1.00		6
	MOTA	7661	0		E 139	66.572	33.826	32.527	1.00		8
	ATOM	7662	N		E 140	68.264	34.770	31.410	1.00		7
	MOTA	7663	CA		E 140	67.449	35.013	30.229	1.00		6
50	ATOM	7664	CB		E 140	66.995	36.513	30.165	1.00	51.60	6 6
	MOTA	7665			E 140 E 140	66.543 68.136	36.974 37.434	31.546 29.766	1.00		6
	ATOM	7666 7667			E 140	.67.815	38.915	30.060		55.62	6
	MOTA MOTA	7668	CDI		E 140	68.145	34.594	28.935		51.13	6
55	ATOM	7669	0		E 140	69.295	34.917	28.710		49.59	8
	ATOM	7670	N		E 141	67.434	33.840	28.102		52.11	7
	MOTA	7671	CA		E 141	67.985	33.382	26.833		51.58	6
	MOTA	7672	С		E 141	66.884	33.089	25.826		51.56	6
	MOTA	7673	0		E 141	65.709	33.125	26.186		52.84	8
60	MOTA	7674	N		E 142	67.245	32.807	24.573		49.52	7
	MOTA	7675	CA	SER	E 142	66.241	32.514	23.553	1.00	46.89	6

	WO 01/58	8951				•			PCT/E	P01/014	57
						-198					•
	MOTA	7676	СВ	SER E	142		32.177	22.214	1 00	44 27	_
	ATOM	7677	OG	SER E			31.657	21.329	1.00		6
	ATOM	7678	C	SER E			31.346	23.997	1.00		8
	ATOM	7679	ō	SER E			30.376	24.584	1.00		6 8
5	ATOM	7680	N.	TRP E			31.439	23.701	1.00		
	MOTA	7681	CA	TRP E			30.406	24.101	1.00		7 6
	ATOM	7682	СВ	TRP E			31.025	24.101	1.00		6
	ATOM	7683	CG	TRP E			30.096	24.968	1.00		6
	ATOM	7684		TRP E			29.697	26.337	1.00		6
10	MOTA	7685	CE2				28.803	26.505	1.00		6
	ATOM	7686	CE3				30.008	27.442	1.00		6
	ATOM	7687		TRP E			29.448	24.371	1.00		6
	ATOM	7688	NE1				28.669	25.288	1.00		7
	ATOM	7689	CZ2				28.216	27.736	1.00		6
15	MOTA	7690	CZ3				29.426	28.662	1.00		6
	ATOM	7691	CH2	TRP E			28.540	28.799	1.00		6
	ATOM	7692	С	TRP E			29.281	23.097	1.00		6
	ATOM	7693	0	TRP E			28.147	23.467	1.00		8
	ATOM	7694	N	THR E			29.579	21.821	1.00		7
20	MOTA	7695	CA	THR E	144		28.539	20.808	1.00		6
	MOTA	7696	CB	THR E			28.863	19.859	1.00		6
	ATOM	7697		THR E			30.174	19.308	1.00 4		8
	ATOM	7698		THR E			28.824	20.609	1.00		6
	MOTA	7699	С	THR E			28.276	19.969	1.00 4		6
25	ATOM	7700	0	THR E		64.434	27.294	19.243	1.00		. 8
	MOTA	7701	N		145	65.367	29.151	20.060	1.00 4		7
	MOTA	7702	CA	HIS E	145	66.576	28.973	19.275	1.00 5		6
	MOTA	7703	CB	HIS E	145	66.937	30.265	18.541	1.00 4		6
	MOTA	7704	CG	HIS E	145	65.947	30.669	17.492	1.00 4		6
30	MOTA	7705	CD2	HIS E	145	65.676	30.143	16.275	1.00 4		6
	MOTA	7706	ND1	HIS E	145	65.112	31.756	17.634	1.00 4		7
	MOTA	7707	CE1	HIS E	145	64.371	31.883	16.548	1.00 4		6
	MOTA	7708	NE2	HIS E	145	64.694	30.917	15.708	1.00 5		7
	MOTA	7709	C	HIS E	145	67.754	28.529	20.125	1.00 5		6
35	MOTA	7710	0	HIS E	145	68.096	29.153	21.129	1.00 5		8
	ATOM	7711	N .	HIS E		68.371	27.427	19.710	1.00 5	55.46	7
	MOTA	7712	CA	HIS E	146	69.530	26.886	20.418	1.00 5	7.69	6
	MOTA	7713	CB	HIS E		69.654	25.377	20.162	1.00 5	6.07	6
40	MOTA	7714	CG	HIS E		69.679	25.019	18.715	1.00 5	6.24	6
40	ATOM	7715		HIS E		70.477	25.442	17.707	1.00 5	55.97	6
	MOTA	7716		HIS E		68.798	24.121	18.157	1.00 5	8.10	7
	ATOM	7717		HIS E		69.053	24.005	16.863	1.00 5	8.23	6
	MOTA	7718		HIS E		70.068	24.797	16.566	1.00 5	7.28	7
45	MOTA	7719	C	HIS E		70.801	27.612	19.971	1.00 5	8.37	6
45	MOTA	7720	0	HIS E		70.775	28.455	19.064	1.00 5	9.37	8
	ATOM	7721	N	SER E		71.908	27.269	20.618	1.00 6	0.00	7
	MOTA	7722	CA	SER E		73.218	27.872	20.356	1.00 6	0.54	6
	MOTA	7723	CB	SER E		74.268	27.134	21.185	1.00 6	0.36	б
EΛ	ATOM	7724	OG	SER E		74.082	25.728	21.071	1.00 6	1.90	8
50	ATOM	7725	С	SER E			27.960	18.897	1.00 6	0.61	6
	MOTA	7726	0	SER E		74.491	28.837	18.553	1.00 6	0.32	8
	ATOM	7727	N	ARG E			27.072	18.041	1.00 5	9.60	7
	ATOM	7728	CA	ARG E			27.083	16.646	1.00 6		6
55	MOTA	7729	CB	ARG E			25.722	15.996	1.00 6		6
J	ATOM	7730	CG	ARG E			24.527	16.756	1.00 7		6
	MOTA	7731	CD	ARG E			23.177	16.169	1.00 7		6
	MOTA	7732	NE	ARG E			22.052	17.077	1.00 8		7
	MOTA	7733	CZ	ARG E			21.680	17.475	1.00 8		6
60	MOTA MOTA	7734		ARG E			22.338	17.046	1.00 8		7
50	ATOM	7735 7736	NH2 C	ARG E			20.650	18.306	1.00 8		7
	ATOM	1130	C	ARG E	TAR	72.942	28.189	15.847	1.00 5	9.62	6

	WO 01/58	951								PCT/EP01/01	457
							-199				
	MOTA	7737	0	ARG	E	148	73.418	28.564	14.766	1.00 58.11	8
	ATOM	7738	N	GLU			71.836	28.707	16.384	1.00 58.68	7
	ATOM	7739	CA	GLU			71.067	29.756	15.716	1.00 56.72	. 6
	ATOM	7740	СВ	GLU			69.598	29.337	15.630	1.00 55.99	6
5	MOTA	7741	CG	GLU			69.435	27.854	15.335	1.00 57.25	6
	ATOM	7742	CD	GLU			67.992	27.402	15.239	1.00 57.65	6
	MOTA	7743		GLU			67.166	27.825	16.075	1.00 58.97	8
	ATOM	7744	OE2				67.684	26.606	14.332	1.00 56.32	8
	MOTA	7745	С	GLU	E	149	71.214	31.073	16.463	1.00 55.95	6
10	MOTA	7746	0	GLU	E	149	71.423	32.122	15.852	1.00 54.41	8
	ATOM	7747	N	ILE			71.109	31.012	17.787	1.00 55.27	7
	ATOM	7748	CA	ILE	E	150	71.265	32.202	18.600	1.00 54.72	6
	ATOM	7749	CB	ILE	E	150	69.922	32.686	19.227	1.00 54.60	6
	MOTA	7750	CG2	ILE	E	150	70.190	33.711	20.339	1.00 51.29	6
15	MOTA	7751	CG1	ILE	E	150	69.051	33,354	18.167	1.00 53.90	6
	MOTA	7752	CD1	ILE	E	150	67.738	33.855	18.709	1.00 52.06	6
	MOTA	7753	C	ILE	E	150	72.238	31.954	19.728	1.00 55.47	6
	MOTA	7754	0	ILE	E	150	72.226	30.898	20.361	1.00 54.39	8
	MOTA	7755	N	SER			73.083	32.948	19.962	1.00 56.26	7
20	MOTA	7756	CA	SER			74.055	32.898	21.035	1.00 59.09	б
	ATOM	7757	CB	SER		_	75.478	32.752	20.471	1.00 59.25	6
	MOTA	7758	OG	SER			75.826	33.853	19.653	1.00 59.55	8
	MOTA	7759	С	SER			73.904	34.226	21.770	1.00 59.98	6
^-	MOTA	7760	0	SER			73.793	35.283	21.139	1.00 59.94	8
25	MOTA	7761	N	VAL			73.878	34.172	23.096	1.00 60.88	7
	ATOM	7762	CA	VAL			73.739	35.380	23.900	1.00 62.73	6
	MOTA	7763	CB	VAL			72.628	35.233	24.956	1.00 61.31	6
	MOTA	7764		VAL			71.339	34.777	24.294	1.00 58.78	6
30	MOTA	7765		VAL			73.067	34.241	26.034	1.00 62.59	6
30	ATOM ATOM	7766 7767	C	VAL VAL			75.054	35.633	24.612	1.00 64.27	6
	ATOM	7768	O NT	ASP			75.743	34.687	24.994	1.00 63.76	8
	ATOM	7769	N CA	ASP			75.393 76.650	36.904	24.805	1.00 66.67	7
	ATOM	7770	CB	ASP			77.713	37.261 37.471	25.456 24.381	1.00 70.32	6
35	ATOM	7771	CG	ASP			77.832	36.272	23.433	1.00 70.77	6 6
00	ATOM	7772		ASP			78.483	35.261	23.433	1.00 74.19	8
	ATOM	7773		ASP			77.265	36.331	22.319	1.00 73.45	8
	ATOM	7774	C	ASP			76.531	38.533	26.304	1.00 73.43	6
	ATOM	7775	ō	ASP			75.835	39.481	25.922	1.00 72.90	8
40	MOTA	7776	N	PRO			77.187	38.561	27.478	1.00 73.33	7
	ATOM	7777	CD	PRO			77.671	37.398	28.243	1.00 72.54	6
	ATOM	7778	CA	PRO	E	154	77.123	39.755	28.332	1.00 75.06	6
	ATOM	7779	CB	PRO			77.749	39,279	29.642	1.00 74.00	6
	MOTA	7780	CG	PRO	E	154	77.389	37.823	29.676	1.00 74.05	6
45	MOTA	7781	С	PRO	E	154	77.911	40.901	27.688	1.00 77.63	6
	ATOM	7782	0	PRO	E	154	78.502	40.717	26.620	1.00 78.05	8
	ATOM	7783	N	THR			77.940	42.066	28.338	1.00 81.26	7
	ATOM	7784	CA	THR			78.638	43.230	27.781	1.00 85.03	6
	ATOM	7785	СВ	THR			77.623	44.147	27.020	1.00 83.83	6
50	MOTA	7786		THR			76.717	44.749	27.956	1.00 81.33	.8
	MOTA	7787		THR			76.815	43.341	26.020	1.00 83.47	б
	MOTA	7788	C	THR			79.417	44.101	28.803	1.00 88.40	6
	ATOM	7789	0	THR			79.900	43.592	29.825	1.00 88.82	8
55	ATOM	7790	N	THR			79.527	45.405	28.487	1.00 91.48	7
J	ATOM	7791	CA	THR			80.206	46.443	29.288	1.00 93.55	6
	ATOM	7792	CB OC1	THR			79.615	47.854	29.002	1.00 93.31	٠ 6
	MOTA	7793		THR			79.697	48.136	27.596	1.00 92.71	8
	ATOM ATOM	7794 7795	CGZ	THR			80.376	48.925	29.813	1.00 92.25	6
60	ATOM	7796	0	THR			80.165 79.173	46.249 46.584	30.803 31.476	1.00 95.69 1.00 95.92	6 8
	ATOM	7797	N	GLU			81.264	45.733	31.340	1.00 93.92	8 7
					_	,	0204		27.240		,

	WO 01/58	8951							PCT	/ <b>EP</b> 01/01	457
						-200					
	ATOM	7798	CA	GLU E	157	81.365	45.481	32.776	1.001	00.21	6
	ATOM	7799	CB	GLU E		82.361	44.343	33.018	1.001		6
	ATOM	7800	CG	GLU E		82.198	43.190	32.046		03.80	б
	MOTA	7801	CD	GLU F		83.222	42.107	32.296	1.001	05.78	6
5	MOTA	7802		GLU E		84.423	42.466	32.375	1.001	05.64	8
_	ATOM	7803		GLU I		82.828	40.907	32.410	1.001	07.35	8
	ATOM	7804	C	GLU E		81.817	46.729	33.550	1.001	00.48	6
•	MOTA	7805	0	GLU I		81.869	46.719	34.798	1.001	00.82	8
	ATOM	7806	N	ASN I	£ 158	82.151	47.793	32.818		99.54	7
10	MOTA	7807	CA	ASN I	158	82.620	49.011	33,461	1.00	98.41	6
	MOTA	7808	CB	ASN I	158	83.235	49.953	32.426		.00.23	6
	MOTA	7809	CG	ASN I	158	84.338	49.283	31.604		.01.57	6
	ATOM	7810		ASN I		85.334	48.768	32.152		00.21	8
	MOTA	7811		ASN I		84.165	49.286	30.274		.02.69	7
15	MOTA	7812	С	ASN I		81.456	49.701	34.156		96.86	6
	MOTA	7813	0	ASN I		81.185	49.443	35.341		96.41	8
.•	MOTA	7814	N		₹ 159	80.791	50.578	33.395		94.72	7
	ATOM	7815	CA		159	79.624	51.349	33.834		91.39	6
20	ATOM	7816	CB		I 159	78.465	51.087	32.858		91.87 92.44	6 8
20	ATOM	7817	OG		± 159	78.391 79.169	49.705	32.499		88.56	6
	MOTA	7818	C		E 159 E 159	78.823	51.080 49.947	35.269 35.614		89.22	8
	MOTA	7819	0		E 160	79.171	52.119	36.102		85.19	7
	MOTA MOTA	7820 7821	N CA	ASP I		78.744	51.966	37.495		81.21	6
25	ATOM	7821	CB		E 160	78.527	53.327	38.157		80.51	6
20	ATOM	7823	CG		E 160	78.005	53.194	39.574		79.98	6
	ATOM	7824		ASP 1		77.424	54.174	40.079		80.37	8
	ATOM	7825		ASP 1		78.184	52.104	40.178		78.39	8
	ATOM	7826	C		E 160	77.426	51.202	37.525		78.59	6
30	ATOM	7827	ō		E 160	76.427	51.669	36.959	1.00	77.98	8
	ATOM	7828	N		E 161	77.427	50.043	38.185	1.00	75.05	7
	ATOM	7829	CA		E 161	76.233	49.203	38.283	1.00	71.67	6
	MOTA	7830	CB	ASP 3	E 161	76.473	48.017	39.226	1.00	70.39	- 6
	MOTA	7831	CG	ASP :	E 161	77.428	46.994	38.641		70.69	6
35	MOTA	7832		ASP 3		77.389	46.782	37.416		70.97	8
	MOTA	7833		ASP :		78.211	46.386	39.400		71.91	8
	MOTA	7834	С		E 161	74.968	49.931	38.732		70.49	6
	MOTA	7835	0		E 161	73.864	49.439	38.514		71.58	8
40	MOTA	7836	N		E 162	75.099	51.093	39.356		68.11	7
40	ATOM	7837	CA		E 162	73.903	51.792	39.785		66.58	6
	ATOM	7838	CB		E 162	73.771	51.731	41.308 41.938		66.49	6 8
	ATOM	7839	OG		E 162 E 162	74.786 73.856	52.478 53.237	39.319		64.63 65.96	6
	ATOM ATOM	7840 7841	O .		E 162	73.050	54.088	39.972		64.77	8
45	ATOM	7842	N		E 163	74.475	53.514	38.178		65.61	7
	MOTA	7843	CA		E 163	74.474	54.872	37.676		67.53	· 6
	MOTA	7844	CB		E 163	75.582	55.051	36,631		70.35	6
	ATOM	7845	CG		E 163	75.237	54.661	35.213		72,94	6
	MOTA	7846	CD		E 163	76.338	55.083	34.225		76.12	6
50	ATOM	7847			E 163	77.424	54.448	34.241	1.00	77.12	8
	ATOM	7848	OE2	GLU	E 163	76.118	56.054	33.445		76.02	8
	ATOM	7849	С	GLU	E 163	73.108	55.271	37.113		66.26	6
	MOTA	7850	0	GLU	E 163	72.873	56.442	36.800		64.91	8
	ATOM	7851	N		E 164	72.211	54.292	36.990		66.34	7
55	MOTA	7852	CA		E 164	70.848	54.539	36.496		65.02	6
	MOTA	7853	CB		E 164	70.555	53.716	35.235		64.40	6
	ATOM	7854	CG		E 164	71.386		34.051		64.81	6
	MOTA	7855			E 164	72.237		33.437		64.72	6
60	MOTA	7856			E 164	73.040	53.559	32.351		65.69	6
60	MOTA	7857			E 164	71.350		33.559 32.471		67.21 67.79	6 6
	MOTA	7858	CEZ	TIK	E 164	72.154	22.003	J2.411	1.00	51.13	. 0

	WO 01/58	8951							PCT/EP01/0	1457
						-201				
	ATOM	7859	CZ	TYR I	3 164	72.994	54.867	31.867	1.00 67.33	6
	ATOM	7860	OH	TYR I		73.744	55.230	30.765	1.00 67.72	8
	ATOM	7861	C	TYR I		69.831	54.174	37.574	1.00 63.42	6
	ATOM	7862	Ō	TYR I		68.642	54.458	37.442	1.00 62.96	8
5	ATOM	7863	N	PHE I		70.309	53.552	38.646	1.00 60.43	7
-	ATOM	7864	CA	PHE 1		69.428	53.139	39.717	1.00 59.92	6
	ATOM	7865	СВ	PHE		70.208	52.378	40.776	1.00 58.36	. 6
	ATOM	7866	CG	PHE 1		69.347	51.515	41.645	1.00 58.01	6
	ATOM	7867		PHE I	<b>≅ 165</b>	68.674	50.427	41.110	1.00 55.31	6
10	ATOM	7868	CD2	PHE 1	E 165	69.189	51.802	42.994	1.00 58.36	6
	MOTA	7869	CE1	PHE 1	E 165	67.858	49.642	41.904	1.00 56.74	6
	ATOM	7870	CE2	PHE I	E 165	68.368	51.016	43.804	1.00 57.34	6
	ATOM	7871	CZ	PHE 1	E 165	67.703	49.939	43.260	1.00 57.55	6
	ATOM	7872	С	PHE !	E 165	68.732	54.324	40.356	1.00 60.15	6
15	MOTA	7873	0	PHE 1	E 165	69.321	55.390	40.504	1.00 62.59	8
	MOTA	7874	N	SER	E 166	67.466	54.148	40.718	1.00 59.42	7
	MOTA	7875	CA	SER :	E 166	66.724	55.222	41.357	1.00 57.86	6
	ATOM	7876	CB	SER :	E 166	65.241	54.869	41.503	1.00 56.65	6
	MOTA	7877	OG		E 166	64.513	55.951	42.064	1.00 53.76	8
20	MOTA	7878	C	SER :	E 166	67.325	55.425	42.733	1.00 56.88	б
	ATOM	7879	0		E 166	67.712	54.472	43.407	1.00 55.76	8
	ATOM	7880	N		E 167	67.406	56.677	43.142	1.00 56.96	7
	MOTA	7881	CA		E 167	67. <u>9</u> 55	57.010	44.443	1.00 58.28	6
	MOTA	7882	CB		E 167	68.547	58.423	44.401	1.00 60.41	6
25	ATOM	7883	CG		E 167	67.549	59.465	43.941	1.00 64.41	6
	ATOM	7884	CD		E 167	68.198	60.780	43.599	1.00 66.50	6
	ATOM	7885		GLM :		68.795	61.433	44.458	1.00 67.54	8
	ATOM	7886	NE2		E 167	68.089	61.184	42.330	1.00 68.48	7
00	MOTA	7887	C		E 167	66.880	56.924	45.532	1.00 57.21	6
30	ATOM	7888	0		E 167	67.196	56.835	46.720	1.00 56.91	8
	ATOM	7889	N		E 168	65.613	56.932	45.133	1.00 54.47	7
	ATOM	7890	CA		E 168	64.550	56.877	46.111	1.00 53.18	6
	ATOM	7891	CB	TYR	E 168	63.399	57.760	45.649	1.00 53.95 1.00 53.27	6 6
35	MOTA	7892	CG CD1			63.881	59.125 59.439	45.249 43.913	1.00 53.27	6
55	ATOM	7893 7894		TYR TYR		64.102 64.625	60.672	43.541	1.00 54.37	6
	MOTA MOTA	7895	CD2		E 168	64.190	60.077	46.208	1.00 50.01	
	ATOM	7896	CE2		E 168	64.711	61.304	45.856	1.00 55.52	6
	ATOM	7897	CEZ		E 168	64.929	61.599	44.522	1.00 57.20	
40	ATOM	7898	ОН	TYR		65.458	62.815	44.177	1.00 59.36	
-10	ATOM	7899	C		E 168	64.072	55.470	46.431	1.00 52.65	6
	ATOM	7900	Ö		E 168	63.131	55.282	47.189	1.00 53.48	8
	MOTA	7901	N		E 169	64.735	54.479	45.861	1.00 51.93	7
	ATOM	7902	CA		E 169	64.387	53.093	46.117	1.00 53.34	
45	ATOM	7903	СВ		E 169	65.191	52.167	45.201	1.00 53.89	6
	ATOM	7904	OG	SER	E 169		50.807	45.514	1.00 50.40	
	MOTA	7905	С		E 169	64.686	52.726	47.567	1.00 54.98	
	ATOM	7906	0		E 169	65.636	53.225	48.162	1.00 54.67	8
	MOTA	7907	N	ARG	E 170	63.875	51.844	48.131	1.00 56.35	
50	ATOM	7908	CA	ARG	E 170	64.075	51.404	49.500	1.00 56.22	6
	MOTA	7909	CB	ARG	E 170	62.869	50.568	49.963	1.00 57.55	6
	MOTA	7910	CG	ARG	E 170	61.832	51.361	50.724	1.00 59.10	
	ATOM	7911	CD		E 170		50.785	50.587	1.00 63.93	
	MOTA	7912	NE		E 170		49.382	50.992	1.00 67.80	
55	MOTA	7913	CZ		E 170		48.405	50.181	1.00 68.39	
	MOTA	7914			E 170		48.664	48.916	1.00 66.05	
	MOTA	7915			E 170		47.163	50.637	1.00 71.45	
	MOTA	7916	С		E 170		50.563	49.577	1.00 56.43	
00	ATOM	7917	0		E 170		50.334	50.666	1.00 57.41	
60	MOTA	7918	N		E 171		50.115	48.423	1.00 54.16	
	MOTA	7919	CA	PHE	E 171	67.011	49.265	48.403	1.00 53.05	6

	WO 01/58	951								PCT/I	E <b>P</b> 01/01	457
							-202					_
	MOTA	7920	CB	PHE			66.665	47.926	47.747	1.00 5		6
	MOTA	7921	CG	PHE			65.392	47.326	48.259	1.00 5		6
	MOTA	7922 7923		PHE			64.157 65.416	47.848 46.288	47.876 49.180	1.00 5		6 6
5	MOTA MOTA	7923 7924		PHE PHE			62.963	47.346	49.100	1.00		6
9	ATOM	7925		PHE			64.233	45.781	49.719	1.00		· 6
	ATOM	7926	CZ	PHE			63.008	46.313	49.334	1.00		6
	ATOM	7927	C	PHE			68.181	49.909	47.698	1.00		6
	ATOM	7928	0	PHE			68.056	50.993	47.137	1.00		8
10	MOTA	7929	N	GLU			69.328	49.245	47.749	1.00		7
	MOTA	7930	CA	GLU	E	172	70.520	49.755	47.106	1.00 5	56.51	6
	MOTA	7931	CB	GLU	E	172	71.385	50.513	48.120	1.00 5		6
	MOTA	7932	CG	GLU			71.906	49.691	49.299	1.00		6
4 ~	MOTA	7933	CD	GLU			72.716	50.527	50.300	1.00		6
15	MOTA	7934		GLU			73.450	51.439	49.861	1.00		8
	ATOM	7935	OE2	GLU			72.635	50.266	51.526	1.00		8
	MOTA	7936	C	GLU			71.288	48.596	46.490 46.917	1.00 !		6 8
	ATOM ATOM	7937 7938	O N	GLU ILE			71.161 72.077	47.451 48.891	45.470	1.00		7
20	ATOM	7939	N CA	ILE			72.844	47.850	44.802	1.00	•	6
20	ATOM	7940	CB	ILE			72.863	48.063	43.274	1.00		6
	ATOM	7941	CG2				73.751	47.016	42.617	1.00		6
	MOTA	7942		ILE			71.439	47.999	42.722	1.00		6
	MOTA	7943		ILE			71.357	48.283	41.245	1.00	60.88	6
25	MOTA	7944	С	ILE			74.289	47.760	45.275	1.00	60.89	6
	MOTA	7945	0	ILE	E	173	75.011	48.752	45.342	1.00	60.64	8
	MOTA	7946	N	LEU			74.715	46.555	45.595	1.00		7
	MOTA	7947	CA	LEU			76.079	46.360	46.019	1.00		6
00	MOTA	7948	СВ	LEU			76.152	45.176	46.968	1.00		6
30	MOTA	7949	CG	LEU			75.126	45.262	48.086	1.00		6
	MOTA	7950		LEU			75.212	44.013	48.952	1.00		6
•	MOTA	7951		LEU			75.367	46.538 46.093	48.896 44.760	1.00		6 6
	MOTA MOTA	7952 7953	C O	LEU			76.908 77.891	46.093	44.780	1.00		8
35	ATOM	7954	N	ASP			76.494	45.102	43.979	1.00		7
00	MOTA	7955	CA	ASP			77.227	44.772	42.763	1.00		6
	ATOM	7956	СВ	ASP			78.496	43.999	43.148	1.00		6
	ATOM	7957	CG	ASP			79.385	43.673	41.961	1.00	67.83	6
	MOTA	7958	OD1	ASP	E	175	79.754	44.600	41.192	1.00	66.66	8
40	MOTA	7959	OD2	ASP			79.727	42.477	41.821	1.00	67.72	8
	MOTA	7960	С	ASP				43.960				6
	MOTA	7961	0	ASP			75.405	43.291	42.216	1.00		. 8
	MOTA	7962	N	VAL			76.692	44.044	40.520	1.00		7
1=	ATOM	7963	CA	VAL			75.974	43.329	39.477	1.00		6
45	ATOM	7964	CB	VAL			75.077	44.283	38.643	1.00 1.00		6
	ATOM	7965 7966		VAL VAL			74.430 74.009	43.524	37.479 39.537	1.00		6 6
	MOTA MOTA	7967	CGZ			176	76.979	42.692	38.541	1.00		6
	MOTA	7968	0	LAV			77.894	43.354	38.078	1.00		8
50	MOTA	7969	N			177	76.796	41.407	38.265	1.00		7
- •	MOTA	7970	CA			177	77.682	40.671	37.362	1.00		6
	MOTA	7971	СВ			177	78.677	39.794	38.142	1.00	69.65	6
	MOTA	7972	OG1	THR	E	177	.77.962	38.938	39.041	1.00	68.82	8
	ATOM	7973	CG2	THR			79.630	40.667	38.938	1.00		6
55	MOTA	7974	С			177	76.870	39.778	36.420	1.00		6
	MOTA	7975	0			177	75.849	39.202	36.813	1.00		8
	MOTA	7976	N			178	77.327	39.669	35.175	1.00		7
	MOTA	7977	CA			178	76.642	38.861	34.173	1.00		6
60	ATOM	7978	CB			178 178	76.151 75.865	39.744 41.187	33.035 33.442	1.00	77.78	6 6
50	ATOM ATOM	7979 7980	CG CD			178	74.935	41.107	32.464	1.00		6
	AT ON	, , , , , ,	CD	٧		_,,	14.233		55.404			U

ATOM 7981 OE1 GLN E 178 75.139 41.862 31.236 1.00 8 ATOM 7982 NE2 GLN E 178 73.909 42.565 33.002 1.00 7 ATOM 7983 C GLN E 178 73.909 42.565 33.002 1.00 7 ATOM 7984 O GLN E 178 77.608 37.840 33.610 1.00 7 ATOM 7985 N LYS E 179 77.248 36.563 33.703 1.00 7 ATOM 7986 CA LYS E 179 78.166 38.205 33.086 1.00 7 ATOM 7987 CE LYS E 179 78.166 34.692 34.391 1.00 7 ATOM 7988 CG LYS E 179 78.166 34.692 34.391 1.00 7 ATOM 7989 CD LYS E 179 79.186 35.600 35.515 1.00 8 ATOM 7999 CC LYS E 179 79.593 34.805 36.763 1.00 8 ATOM 7991 NZ LYS E 179 79.593 34.805 36.763 1.00 8 ATOM 7991 NZ LYS E 179 79.593 34.805 36.763 1.00 8 ATOM 7991 NZ LYS E 179 79.779 35.727 37.981 1.00 8 ATOM 7992 C LYS E 179 77.274 34.554 32.353 1.00 7 ATOM 7993 O LYS E 179 77.274 34.554 32.353 1.00 7 ATOM 7994 N LYS E 180 77.274 34.554 32.353 1.00 7 ATOM 7995 CA LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7996 CB LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7997 CG LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 7998 CD LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 7999 CC LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 7998 CD LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8006 CB ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8007 OD1 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 CB ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 C ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 C ASN E 181 75.658 28.92 29.097 1.00 7 ATOM 8013 CB SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8010 C SE	78.21 74.50 74.89 75.28 75.34 77.30 81.23 83.79 82.45 74.24 74.20 72.18 70.93 71.21 67.95 66.39 67.24 69.92 70.33	876876666676876666676
ATOM 7982 NE2 GLN E 178 73.909 42.565 33.002 1.00 7 ATOM 7983 C GLN E 178 77.608 37.840 33.610 1.00 7 ATOM 7984 O GLN E 178 78.661 38.205 33.086 1.00 7 ATOM 7985 N LYS E 179 77.248 36.563 33.703 1.00 7 ATOM 7986 CA LYS E 179 78.107 35.482 33.209 1.00 7 ATOM 7987 CB LYS E 179 78.666 34.692 34.391 1.00 7 ATOM 7988 CG LYS E 179 79.186 35.600 35.515 1.00 8 ATOM 7989 CD LYS E 179 79.186 35.600 35.515 1.00 8 ATOM 7990 CE LYS E 179 79.186 35.600 35.515 1.00 8 ATOM 7990 CE LYS E 179 79.797 35.727 37.981 1.00 8 ATOM 7991 NZ LYS E 179 79.797 35.727 37.981 1.00 8 ATOM 7991 NZ LYS E 179 79.779 35.727 37.981 1.00 8 ATOM 7992 C LYS E 179 77.274 34.554 32.353 1.00 7 ATOM 7993 O LYS E 179 77.274 34.554 32.353 1.00 7 ATOM 7993 O LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7995 CA LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7996 CB LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7996 CB LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7997 CG LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 7997 CG LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 7999 CC LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.062 34.017 28.694 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8001 CC LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8001 CC ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8001 CC ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8000 NZ LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8001 CC ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8001 CC ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8001 CC	78.21 74.50 74.89 75.28 75.34 77.30 81.23 83.79 82.45 74.24 74.20 72.18 70.93 71.21 67.95 66.39 67.24 69.92 70.33	7687666667687666667
ATOM 7983 C GLN E 178	74.50 6 74.89 8 75.28 7 75.34 6 77.30 6 81.23 6 83.79 6 82.45 7 74.24 6 74.20 8 70.93 6 71.21 6 67.95 6 66.39 6 67.24 6 69.92 7 70.33 6	687666667687666667
ATOM         7984         O         GLN         E         178         78.661         38.205         33.086         1.00         7           ATOM         7985         N         LYS         E         179         77.248         36.563         33.703         1.00         7           ATOM         7987         CB         LYS         E         179         78.666         34.692         34.391         1.00         7           ATOM         7988         CG         LYS         E         179         79.186         35.600         35.515         1.00         8           ATOM         7990         CE         LYS         E         179         79.593         34.805         36.763         1.00         8           ATOM         7990         CE         LYS         E         179         79.593         34.805         36.763         1.00         8           ATOM         7991         NZ         LYS         E         179         77.524         34.533         31.00         8         1.00         7           ATOM         7994         N         LYS         E         180         77.524         34.533         31.045         1.00	74.89 8 75.28 7 75.34 6 77.30 6 81.23 6 83.79 6 82.45 7 74.24 6 74.20 8 70.93 6 71.21 6 67.95 6 66.39 6 67.24 6 69.92 7 70.33 8	87666667687666667
ATOM	75.28 75.34 77.30 81.23 83.79 82.73 82.45 74.24 74.20 72.18 70.93 71.21 67.95 66.39 67.24 69.92 70.33	7666667687666667
ATOM 7986 CA LYS E 179	75.34 67.30 681.23 683.79 682.45 674.24 674.20 8774.20 8774.21 67.95 67.85 66.39 67.24 69.92 70.33	666667687666667
ATOM 7987 CB LYS E 179 78.6666 34.692 34.391 1.00 7 ATOM 7988 CG LYS E 179 79.186 35.600 35.515 1.00 8 ATOM 7989 CD LYS E 179 79.593 34.805 36.763 1.00 8 ATOM 7990 CE LYS E 179 79.593 34.805 36.763 1.00 8 ATOM 7991 NZ LYS E 179 79.779 35.727 37.981 1.00 8 ATOM 7992 C LYS E 179 77.274 34.554 32.353 1.00 7 ATOM 7993 O LYS E 179 76.409 33.850 32.882 1.00 7 ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7995 CA LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7996 CB LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7997 CG LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7998 CD LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 8000 NZ LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.535 31.310 29.711 1.00 6 ATOM 8004 CA ASN E 181 76.550 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8006 CG ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8007 ODI ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 O ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8011 N SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8011 N SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7	77.30 (81.23 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83	66667687666667
ATOM 7988 CG LYS E 179	81.23 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83.79 (83	6667687666667
10 ATOM 7989 CD LYS E 179 79.593 34.805 36.763 1.00 8 ATOM 7990 CE LYS E 179 79.779 35.727 37.981 1.00 8 ATOM 7991 NZ LYS E 179 78.496 36.431 38.332 1.00 8 ATOM 7992 C LYS E 179 76.409 33.850 32.882 1.00 7 ATOM 7993 O LYS E 179 76.409 33.850 32.882 1.00 7 ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7995 CA LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7996 CB LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7997 CG LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7998 CD LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.005 32.722 25.197 1.00 6 ATOM 8000 NZ LYS E 180 77.049 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.049 32.099 30.429 1.00 6 ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 O ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8016 O SER E 182 75.512 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 29.956 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 29.955 1.00 6	83.79 (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79) (83.79)	667687666667
10 ATOM 7990 CE LYS E 179 79.779 35.727 37.981 1.00 8     ATOM 7991 NZ LYS E 179 78.496 36.431 38.332 1.00 8     ATOM 7992 C LYS E 179 77.274 34.554 32.353 1.00 7     ATOM 7993 O LYS E 179 76.409 33.850 32.882 1.00 7     ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7     ATOM 7995 CA LYS E 180 76.747 33.674 30.155 1.00 7     ATOM 7996 CB LYS E 180 76.747 33.674 30.155 1.00 7     ATOM 7997 CG LYS E 180 77.062 34.017 28.694 1.00 7     ATOM 7998 CD LYS E 180 78.412 33.558 28.187 1.00 6     ATOM 7999 CE LYS E 180 78.422 33.558 28.187 1.00 6     ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6     ATOM 8000 NZ LYS E 180 77.429 32.041 26.394 1.00 6     ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6     ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6     ATOM 8003 N ASN E 181 76.335 31.310 29.878 1.00 7     ATOM 8004 CA ASN E 181 76.563 29.495 31.362 1.00 6     ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 6     ATOM 8007 OD1 ASN E 181 76.563 29.495 31.362 1.00 6     ATOM 8009 C ASN E 181 75.659 30.060 32.112 1.00 7     ATOM 8009 C ASN E 181 75.659 30.060 32.112 1.00 7     ATOM 8009 C ASN E 181 75.659 30.060 32.112 1.00 7     ATOM 8009 C ASN E 181 75.659 30.066 32.112 1.00 7     ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7     ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7     ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7     ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7     ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7     ATOM 8013 CB SER E 182 75.512 25.836 29.428 1.00 7     ATOM 8014 CG SER E 182 75.512 25.836 29.428 1.00 7     ATOM 8015 C SER E 182 75.527 25.836 29.428 1.00 7     ATOM 8017 N VAL E 183 73.341 24.295 28.738 1.00 7     ATOM 8018 CA VAL E 183 73.341 24.295 29.955 1.00 6     ATOM 8019 CB VAL E 183 73.341 24.295 29.955 1.00 6	32.73 (82.45) (82.45) (82.45) (82.45) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46) (82.46)	6768766667
ATOM 7991 NZ LYS E 179 78.496 36.431 38.332 1.00 8 ATOM 7992 C LYS E 179 77.274 34.554 32.353 1.00 7 ATOM 7993 O LYS E 179 76.409 33.850 32.882 1.00 7 ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7995 CA LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7996 CB LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7997 CG LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7998 CD LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 8000 NZ LYS E 180 78.005 32.722 25.197 1.00 6 ATOM 8000 NZ LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.803 31.876 31.303 1.00 7 ATOM 8003 N ASN E 181 76.533 31.310 29.711 1.00 6 ATOM 8004 CA ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 7 ATOM 8006 CG ASN E 181 75.659 30.060 32.112 1.00 7 ATOM 8007 OD1 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 CG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8016 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7	82.45 74.24 74.20 72.18 70.93 71.21 67.95 66.39 66.39 67.24 69.92 70.33	7687666667
ATOM 7992 C LYS E 179 77.274 34.554 32.353 1.00 7 ATOM 7993 O LYS E 179 76.409 33.850 32.882 1.00 7 ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7995 CA LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7996 CB LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7996 CB LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7997 CG LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.005 32.722 25.197 1.00 6 ATOM 8000 NZ LYS E 180 78.005 32.722 25.197 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.803 31.876 31.303 1.00 7 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8005 CB ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 O ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8011 N SER E 182 75.518 27.161 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 28.236 1.00 7 ATOM 8014 OG SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8015 C SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7	74.24 (74.20 174.20 175.21 (75.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175.21 175	6 8 7 6 6 6 6 6 7
ATOM 7993 O LYS E 179 76.409 33.850 32.882 1.00 7 ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7995 CA LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7996 CB LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7997 CG LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7998 CD LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 8000 NZ LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 8000 NZ LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.535 31.310 29.711 1.00 6 ATOM 8003 N ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.659 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8011 N SER E 182 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8014 OG SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8014 OG SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VA	74.20 177.21 187.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197.21 197	8 7 6 6 6 6 6 6 7
ATOM 7994 N LYS E 180 77.528 34.533 31.045 1.00 7 ATOM 7995 CA LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7996 CB LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7997 CG LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7998 CD LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7999 CE LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 78.005 32.722 25.197 1.00 6 ATOM 8000 NZ LYS E 180 77.0429 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8003 N ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.653 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8000 C ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 CO SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8018 CA VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VALE 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VALE 183	72.18 70.93 71.21 67.95 67.85 66.39 67.24 69.92 70.33	7 6 6 6 6 6 7
15 ATOM 7995 CA LYS E 180 76.747 33.674 30.155 1.00 7 ATOM 7996 CB LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7997 CG LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7998 CD LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8000 NZ LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8003 N ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8008 ND2 ASN E 181 75.595 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8008 ND2 ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8016 O SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8010 CB VAL E	70.93 (71.21 (67.95 (67.85 (66.39 (69.92 (70.33 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69.93 (69	6 6 6 6 7
ATOM 7996 CB LYS E 180 77.062 34.017 28.694 1.00 7 ATOM 7997 CG LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7998 CD LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8000 NZ LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8003 N ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8008 ND2 ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.655 30.066 31.648 1.00 7 ATOM 8008 ND2 ASN E 181 75.655 30.066 31.648 1.00 7 ATOM 8008 ND2 ASN E 181 75.655 30.566 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 75.655 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7 ATOM 8015 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8016 O SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8010 CB VAL E 183 73.341 24.295 28.755 1.00 80 ATOM 8010 CB V	71.21 (67.95 (67.85 (66.39 (69.92 (70.33 (69.92 (70.33 (69.92 (70.33 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69.92 (69	6 6 6 7
ATOM 7997 CG LYS E 180 78.412 33.558 28.187 1.00 6 ATOM 7998 CD LYS E 180 78.327 32.136 27.630 1.00 6 ATOM 7999 CE LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8000 NZ LYS E 180 77.429 32.041 26.394 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.936 25.350 27.914 1.00 7	67.95 67.85 66.39 67.24 69.92 70.33	6 6 6 7
ATOM 7998 CD LYS E 180	67.85 66.39 67.24 69.92 70.33	6 6 7
20 ATOM 8000 NZ LYS E 180 78.005 32.722 25.197 1.00 6 ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.803 31.876 31.303 1.00 7 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8007 OD1 ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 75.658 28.918 29.276 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8015 C SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6	67.24 69.92 70.33	7
ATOM 8001 C LYS E 180 77.014 32.199 30.429 1.00 6 ATOM 8002 O LYS E 180 77.803 31.876 31.303 1.00 7 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8007 OD1 ASN E 181 75.659 30.060 32.112 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6	69.92 70.33	
ATOM 8002 O LYS E 180 77.803 31.876 31.303 1.00 7 ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8007 OD1 ASN E 181 74.255 30.006 31.648 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6	70.33	_
ATOM 8003 N ASN E 181 76.335 31.310 29.711 1.00 6 ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8007 OD1 ASN E 181 74.255 30.006 31.648 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		6
ATOM 8004 CA ASN E 181 76.570 29.881 29.878 1.00 7   ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6   ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7   ATOM 8007 OD1 ASN E 181 74.255 30.006 31.648 1.00 7   ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7   ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7   ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7   ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7   ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7   ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7   ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7   ATOM 8015 C SER E 182 75.712 25.791 25.388 1.00 7   ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7   ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7   ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7   ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6   ATOM 8019 CB VAL E 183 72.582 24.906 29.955 1.00 6	69.75 '	8
25 ATOM 8005 CB ASN E 181 76.563 29.495 31.362 1.00 6 ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8007 OD1 ASN E 181 74.255 30.006 31.648 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		7
ATOM 8006 CG ASN E 181 75.395 30.060 32.112 1.00 7 ATOM 8007 OD1 ASN E 181 74.255 30.006 31.648 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 74.438 28.918 29.276 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8015 C SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 75.512 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		6
ATOM 8007 OD1 ASN E 181 74.255 30.006 31.648 1.00 7 ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 74.438 28.918 29.276 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8015 C SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		6
ATOM 8008 ND2 ASN E 181 75.659 30.587 33.299 1.00 7 ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7 ATOM 8010 O ASN E 181 74.438 28.918 29.276 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8015 C SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8016 O SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		6
ATOM 8009 C ASN E 181 75.658 28.932 29.097 1.00 7  ATOM 8010 O ASN E 181 74.438 28.918 29.276 1.00 7  ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7  ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7  ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7  ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7  ATOM 8015 C SER E 182 75.712 25.791 25.388 1.00 7  ATOM 8016 O SER E 182 74.984 26.054 28.345 1.00 7  ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7  ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7  ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		8
30 ATOM 8010 O ASN E 181 74.438 28.918 29.276 1.00 7 ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7 ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7 ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8015 C SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		7
ATOM 8011 N SER E 182 76.266 28.121 28.236 1.00 7  ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7  ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7  ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7  ATOM 8015 C SER E 182 74.984 26.054 28.345 1.00 7  ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7  ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7  ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7  ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		6
ATOM 8012 CA SER E 182 75.518 27.161 27.427 1.00 7 ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7 ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8015 C SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		8
ATOM 8013 CB SER E 182 76.437 26.566 26.343 1.00 7  ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7  ATOM 8015 C SER E 182 74.984 26.054 28.345 1.00 7  ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7  ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7  ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7  ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		7 6
ATOM 8014 OG SER E 182 75.712 25.791 25.388 1.00 7 ATOM 8015 C SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		6
35 ATOM 8015 C SER E 182 74.984 26.054 28.345 1.00 7 ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		8
ATOM 8016 O SER E 182 75.527 25.836 29.428 1.00 7 ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6		6
ATOM 8017 N VAL E 183 73.936 25.350 27.914 1.00 7 ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6 40 ATOM 8020 CG1 VAL E 183 71.892 26.184 29.555 1.00 6		8
ATOM 8018 CA VAL E 183 73.341 24.295 28.738 1.00 7 ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6 40 ATOM 8020 CG1 VAL E 183 71.892 26.184 29.555 1.00 6		7
ATOM 8019 CB VAL E 183 72.582 24.906 29.956 1.00 6 40 ATOM 8020 CG1 VAL E 183 71.892 26.184 29.555 1.00 6		6
		6
	67.54	6
ATOM 8021 CG2 VAL E 183 71.534 23.922 30.470 1.00 6	69.87	6
ATOM 8022 C VAL E 183 72.366 23.391 27.986 1.00 7		6
ATOM 8023 O VAL E 183 71.508 23.867 27.234 1.00 7		8
ATOM 8024 N THR E 184 72.490 22.087 28.202 1.00 7		7
45 ATOM 8025 CA THR E 184 71.586 21.134 27.551 1.00 7		6
ATOM 8026 CB THR E 184 72.339 19.902 26.988 1.00 7		6
ATOM 8027 OG1 THR E 184 73.243 20.327 25.957 1.00 7		8
ATOM 8028 CG2 THR E 184 71.353 18.897 26.392 1.00 7		6
ATOM 8029 C THR E 184 70.547 20.656 28.565 1.00 7 50 ATOM 8030 O THR E 184 70.862 20.458 29.740 1.00 7		6 8
5U ATOM 8030 O THR E 184 70.862 20.458 29.740 1.00 7 ATOM 8031 N TYR E 185 69.307 20.495 28.110 1.00 7		7
ATOM 8031 N TIR E 185 69.307 20.493 28.110 1.00 7		6
ATOM 8032 CA TIR E 105 68.234 20.034 20.992 1.00 7		6
ATOM 8034 CG TYR E 185 67.547 22.482 29.285 1.00 7		6
55 ATOM 8035 CD1 TYR E 185 68.203 23.218 28.304 1.00 7		6
ATOM 8036 CE1 TYR E 185 68.666 24.506 28.559 1.00 7		6
ATOM 8037 CD2 TYR E 185 67.361 23.065 30.544 1.00 7		6
ATOM 8038 CE2 TYR E 185 67.822 24.359 30.817 1.00 7	79.31	6
ATOM 8039 CZ TYR E 185 68.472 25.075 29.819 1.00 7	79.42	6
60 ATOM 8040 OH TYR E 185 68.919 26.357 30.067 1.00 8		8
ATOM 8041 C TYR E 185 67.725 18.723 28.516 1.00 7	77.68	6

	WO 01/5	8951				004		PCT/EP01/01457				
		0040	_	mar.	- 105	-204 67.578	18.509	27.314	1.00	76 95	8	
	MOTA	8042			E 185 E 186	67.460	17.831	29.463	1.00		7	
	MOTA	8043 8044	N Ca		E 186	66.968	16.497	29.134	1.00		6	
	ATOM ATOM	8044	CA CB		E 186	66.593	15.755	30.423	1.00		6	
5		8045	OG		E 186	65.784	16.580	31.254	1.00		8	
5	MOTA	8047	C		E 186	65.770	16.594	28.192	1.00		. 6	
	ATOM ATOM	8047	0		E 186	65.612	15.764	27.291	1.00		8	
	ATOM	8049	Ŋ		E 187	64.948	17.624	28.402	1.00		7	
	ATOM	8050	CA		E 187	63.753	17.876	27.583	1.00		6	
10	MOTA	8051	C		E 187	64.119	18.104	26.143		83.62	6	
10	MOTA	8052	0		E 187	63.463	17.631	25.206	1.00	82.88	8	
	ATOM	8053	СВ		E 187	63.043	19.179	27.993	1.00	83.49	6	
	ATOM	8054	SG		E 187	63.980	20.757	27.703	1.00	86.50	16	
	ATOM	8055	N		E 188	65.204	18.841	25.993	1.00	84.35	7	
15	ATOM	8056	CA		E 188	65.589	19.318	24.701	1.00	84.60	6	
. •	ATOM	8057	C		E 188	67.013	18.991	24.213		84.20	6	
	ATOM	8058	Ō		E 188	68.012	19.334	24.874		84.71	8	
	ATOM	8059	CB		E 188	65.319	20.833	24.759		85.11	6	
	MOTA	8060	SG	CYS	E 188	63.808	21.349	25.731		88.15	16	
20	MOTA	8061	N		E 189	67.108	18.340	23.025		83.48	7	
	MOTA	8062	CD	PRO	E 189	65.864	18.064	22.267		82.84	6	
	MOTA	8063	CA	PRO	E 189	68.292	17.878	22.267		81.51	6	
	ATOM	8064	CB		E 189	67.738	17.666	20.853		82.30	6	
	MOTA	8065	CG		E 189	66.345	17.173	21.119		82.79	6	
25	MOTA	8066	С		E 189	69.547	18.782	22.249		79.46	6	
	MOTA	8067	0		E 189	70.592	18.398	22.785		79.36	8	
	MOTA	8068	N		E 190	69.450	19.961	21.629		76.55	7	
	MOTA	8069	CA		E 190	70.592	20.878	21.529		74.34	6	
	MOTA	8070	CB		E 190	70.358	21.881	20.401		76.82 80.12	6	
30	MOTA	8071	CG		E 190	69.520	21.352	19.239		81.75	6 6	
	MOTA	8072	CD		E 190	70.336	20.533	18.231		81.85	8	
	ATOM	8073			E 190	71.471	20.965 19.472	17.884 17.775		80.52	8	
	MOTA	8074	OE2		E 190	69.836 70.822	21.663	22.815		71.33	6	
05	MOTA	8075	C		E 190	70.022	21.489	23.791		71.05	8	
35	MOTA	8076	0		E 190 E 191	70.095	22.543	22.798		68.78	7	
	MOTA	8077 8078	N	•	E 191	72.142	23.390	23.957		67.15	6	
	MOTA MOTA	8079	CA CB		E 191	73.651	23.536	24.108		65.15	6	
	ATOM	8080	C		E 191	71.502	24.787	23.836		65.83	6	
40	ATOM	8081	Ö		E 191	71.379	25.340	22.730	1.00	64.00	8	
-10	ATOM	8082	N		E 192	71.097	25.355	24.971	1.00	64.83	7	
	MOTA	8083	CA		E 192	70.487	26.678	24.964	. 1.00	65.12	6	
	ATOM	8084	СВ		E 192	69.025	26.613	25.450		63.81	6	
	MOTA	8085			E 192	68.096	25.953	24.462		63.14	6	
45	MOTA	8086	CD1		E 192	67.939	24.564	24.442		64.40	6	
	ATOM	8087			E 192	67.146	23.934	23.468		64.53	6	
	ATOM	8088	CD2		E 192	67.435	26.705	23.493		62.60	6	
	ATOM	8089	CE2	TYR	E 192	66.642		22.521		64.04	6	
	ATOM	8090	CZ	TYR	E 192	66.505	24.710	22.512		64.71	6	
50	ATOM	8091	OH		E 192	65.744	24.101	21.538		66.46	8	
	MOTA	8092	С		E 192	71.262	27.694	25.795		65.22	6	
,	MOTA	8093	0		E 192	71.181	27.699	27.026		67.13	8	
	ATOM	8094	N		E 193	72.010	28.557	25.112		65.61	7	
	MOTA	8095	CA		E 193	72.792	29.606	25.773		64.70 66.19	6 6	
55	MOTA	8096			E 193	73.643	30.372	24.749		69.50		
	MOTA	8097			E 193	74.722	29.522	24.074		72.29	6	
	ATOM	8098	CD		E 193	75.625	30.345	23.144 23.584		71.70		
	ATOM	8099			E 193	76.083	31.435 29.898	23.504		73.48	. 8	
60	MOTA	8100			E 193 E 193	75.881 71.890	30.600			63.08		
60	MOTA	8101			E 193	70.747	30.828	26.095		64.03		
	MOTA	8102	0	GLU	ביד יי	,	55.526				•	

	WO 01/58	8951				205		PCT/EP01/01457				
	ATOM	8103	N	ASP E	194	-205 72.418	31.187	27.566	1.00	62.00	Ż	
	ATOM	8104	CA	ASP E		71.683	32.168	28.340		60.31	6	
	ATOM	8105	CB	ASP E		70.644	31.480	29.235	1.00		6	
	MOTA	8106	CG	ASP E		71.268	30.749	30.413		64.58	6	
5	ATOM	8107		ASP E		71.200	29.504	30.448		66.44	8	
U	ATOM	8108		ASP E		71.824	31.415	31.314		64.95	8	
	ATOM	8109	C	ASP E		72.637	32.989	29.193		59.18	6	
	ATOM	8110	Ö	ASP E		73.715	32.515	29.570		59.24	8	
	ATOM	8111	N	VAL E		72.238	34.223	29.484	1.00	56.73	7	
10	ATOM	8112	CA	VAL E		73.029	35.121	30.311		55.51	6	
	ATOM	8113	СВ	VAL E		73.019	36.555	29.763		53.92	6	
	ATOM	8114		VAL E		73.686	37.498	30.752	1.00	53.41	6	
	ATOM	8115		VAL E		73.738	36.595	28.431	1.00	55.34	. 6	
	MOTA	8116	C	VAL E		72.453	35.145	31.715	1.00	56.03	6	
15	MOTA	8117	Ō	VAL E		71.270	35.400	31.907	1.00	56.70	8	
	ATOM	8118	N	GLU E		73.292	34.868	32.702	1.00	57.06	7	
	ATOM	8119	CA	GLU E		72.834	34,870	34.077	1.00	57.01	6	
	ATOM	8120	СВ	GLU E		73.402	33.673	34.821	1.00	57.41	6	
	MOTA	8121	CG	GLU E		72.908	33,555	36.238	1.00	61.42	6	
20	MOTA	8122	CD	GLU E		73.533	32.383	36.968	1.00	62.69	6	
	ATOM	8123		GLU E		73.377	31.235	36.493	1.00	64.88	8	
	ATOM	8124	OE2	GLU E		74.184	32.604	38.013	1.00	64.76	8	
	ATOM	8125	С	GLU E		73.315	36.160	34.715	1.00	57.51	6	
	ATOM	8126	0	GLU F		74.518	36.427	34.755	1.00	60.16	8	
25	ATOM	8127	N	VAL E		72.375	36.969	35.192	1.00	55.54	7	
	ATOM	8128	CA	VAL E	197	72.712	38.226	35.829	1.00	54.09	6	
	ATOM	8129	CB	VAL E		71.853	39.380	35.278	1.00	50.90	6	
	ATOM	8130	CG1	VAL E		72.241	40.685	35.932	1.00	47.64	6	
	MOTA	8131		VAL E		72.030	39.471	33.782	1.00	49.59	б	
30	ATOM	8132	С	VAL E		72.473	38.067	37.325		56.97	6	
	ATOM	8133	0	VAL E	197	71.414	37.614	37.748	1.00	58.03	8	
	ATOM	8134	N	SER I		73.476	38.409	38.125	1.00	58.05	7	
	ATOM	8135	CA	SER I	198	73.338	38.300	39.562		58.55	6	
	ATOM	8136	CB	SER I	198	74.550	37.584	40.174		58.65	6	
35	ATOM	8137	OG	SER I	198	74.556	36.209	39.811		60.87	8	
	ATOM	8138	С	SER F	198	73.182	39.685	40.155	1.00	58.53	6	
	ATOM	8139	0	SER E	198	74.049	40.549	40.004		59.57	8	
	MOTA	8140	N	LEU I	199	72.060	39.895	40.823		58.51	7	
	MOTA	8141	CA	LEU I	199	71.803	41.176	41.434		59.74	6	
40	ATOM	8142	CB	LEU E	199	70.361	41.612	41.186		59.28	б	
	MOTA	8143	CG	LEU 1	199	69.921	42.861	41.953	1.00	58.45	6	
	MOTA	8144		PEA 1		70.758		41.543		57.64	6	
	MOTA	8145	CD2	LEU I		68.466		41.669		57.53	б	
	ATOM	8146	С	LEU 1	E 199	72.039		42.917		61.63	б	
45	ATOM	8147	0	LEU 1	199	71.226		43.640		64.16	8	
	MOTA	8148	N	ASN	₹ 200	73.163		43.366		61.69	7	
	MOTA	8149	CA	ASN I		73.486	41,658	44.780		58.91	6	
	MOTA	8150	CB		3 200	74.981		44.994		61.22	6	
	ATOM	8151	CG		E 200	75.355		46.454		63.36	6	
50	MOTA	8152		ASN 1		74.686		47.295		64.82	8	
	ATOM	8153	ND2	ASN 1		76.426		46.770		64.37	7	
	MOTA	8154	С		₹ 200	73.048		45.280		56.95	6	
	MOTA	8155	0		€ 200	73.610		44.905		58.64	8	
	MOTA	8156	N		€ 201	72.018		46.109		54.18	7	
55	ATOM	8157	CA		E 201	71.474		46.650		52.16	6	
	MOTA	8158	CB		E 201	70.257		45.844		50.83	6	
	MOTA	8159	CG		E 201	69.065		46.028		47.47	6	
	MOTA	8160		PHE		67.923		46.681		47.04	6	
~~	MOTA	8161		PHE				45.601		44.93	6	
60		8162		PHE				46.911		45.49	6	
	MOTA	8163	CE2	PHE	E 201	68.043	41.608	45.829	1.00	43.88	6	

	WO 01/58	8951								PCT/EP01/01457				
					_			-206	40.050	45 400		42.06	_	
	ATOM	8164	CZ	PHE		201		66.905 71.029	42.072 43.977	46.488 48.066	_	43.86 53.50	6 6	
	ATOM ATOM	8165 8166	C	PHE PHE				71.029	42.823	48.504	1.00		8	
	ATOM	8167		ARG		202	·	70.650	45.032	48.770	1.00		7	
5	ATOM	8168		ARG		202		70.195	44.915	50.146	1.00		6	
•	ATOM	8169	CB	ARG				71.399	44.898	51.084		59.58	6	
	ATOM	8170		ARG				72.078	46.254	51.130		64.26	6	
	MOTA	8171	CD	ARG		202		73.337	46.278	51.951		65.59	б	
	ATOM	8172	NE	ARG	E	202		73.935	47.606	51.908		67.13	7	
10	ATOM	8173	CZ	ARG		202		75.140	47.891	52.386		68.53	6	
	ATOM	8174		ARG				75.870	46.930	52.942		69.03	7	
	MOTA	8175		ARG				75.612	49.129	52.303		68.11	7	
	MOTA	8176	C	ARG				69.321	46.121	50.499		57.27	6	
4-	ATOM	8177	0	ARG				69.370	47.167	49.839		56.88 56.76	8 7	
15	MOTA	8178	N	LYS				68.528	45.974	51.551		57.10	6	
	MOTA	8179	CA	LYS				67.689 66.755	47.063 46.583	52.011 53.109		58.42	6	
	ATOM ATOM	8180 8181	CB CG	LYS		203		65.904	47.682	53.702		60.29	6	
	ATOM	8182	CD	LYS				65.112	47.157	54.883		64.62	6	
20	ATOM	8183	CE	LYS				64.222	48.241	55.471		67.46	6	
	ATOM	8184	NZ	LYS				63.171	48.696	54.504		70.79	7	
	ATOM	8185	C	LYS				68.623	48.101	52.603	1.00	56.53	6	
	ATOM	8186	0	LYS				69.715	47.769	53.060		58.18	8	
	MOTA	8187	N	LYS	E	204		68.190	49.352	52.629		53.82	7	
25	MOTA	8188	CA	LYS		204		69.021	50.392	53.207		52.45	б	
	ATOM	8189	CB	LYS	E	204		68.545	51.766	52.731		50.86	6	
	MOTA	8190	CG	LYS				68.852	52.110	51.279		44.94	6	
	MOTA	8191	CD	LYS				68.253	53.462	50.970		45.54	6	
~~	MOTA	8192	CE	LYS				68.744	54.050	49.669		46.91	6	
30	MOTA	8193	NZ	LYS				68.388	53.268	48.463		48.94 54.01	7 6	
	MOTA	8194	C	LYS LYS				68.991 68.119	50.317 49.668	54.747 55.329		54.82	8	
	MOTA	8195 8196	N O	GLY				69.958	50.969	55.394		53.51	7	
	MOTA MOTA	8197	CA	GLY				70.025	50.987	56.848		52.96	6	
35	ATOM	8198	C	GLY				69.747	52.400	57.344		54.24	6	
00	ATOM	8199	-	GLY				69.326	53.224	56.507		53.02	8	
	ATOM	8200		GLY				69.937	52.697	58.551		54.73	8	
	ATOM	8201		WAT		1		42.707	26.844	16.535	1.00	50.04	8	
	ATOM	8202	OH2	WAT	W	2		46.115	22.922	8.819		33.72	8	
40	MOTA	8203	OH2	WAT	W	3		49.921	22.962	13.240		27.71	8	
	MOTA	8204	ОН2	WAT	W	4		48.219	24.526	9.434		48.75	8	
	MOTA	8205		TAW		5		27.826	41.690	17.095		41.54	8	
	MOTA	8206		TAW		6		24.872	36.589	8.613		51.20	8	
4=	MOTA	8207		WAT		7		36.046	60.034	17.934		33.21 28.29	8 8	
45	MOTA	8208		WAT		8 9		35.043 55.882	57.811 56.455	16.418 16.997		31.72	8	
	ATOM ATOM	8209 8210		TAW TAW		10		55.717	62.292	9.132		41.99	8	
	ATOM	8211		WAT		11		54.077	57.638	15.628		35.89	8	
	ATOM	8212		WAT		12		60.807	36.700	17.893		31.22	. 8	
50	ATOM	8213		WAT		13		66.541	42.748	13.082	1.00	52.94	8	
- •	ATOM	8214		WAT		14		64.752	41.327	9.587	.1.00	53.75	8	
	ATOM		CA+2	CA2	I	1		56.450	11.097	37.999		76.79	20	
	MOTA		CL-1			2		37.092	21.684	12.754		43.91	17	
_	MOTA	8217	CA+2	CA2	I	3		17.667	23.110	38.506		80.38	20	
55	MOTA		CL-1			4		20.502	44.774	13.190		62.37	17	
	MOTA		CA+2			5		16.762	64.154	38.299		85.82	20	
	MOTA		CL-1			6		37.412	67.363	13.067		45.17	17	
	ATOM		CA+2			7		55.038	76.858	37.301		71.00 69.47	20	
60	ATOM		CL-1			8 9		64.026 79.499	57.746 45.067	12.334 37.836		85.28	17 20	
OU	ATOM ATOM		CA+2 CL-1					64.286	29.844	12.440		48.05	17	
	ATOM	0224	CH-T	CDI	_	10		04.200	27.044	12.340	2.00	-0.03	_,	

	WO 01/5	8951		•					PCT/EP01/01	457
						-207		02 680	1.00109.78	6
	MOTA	8225		HEP L	1	31.694		23.679 25.000	1.00109.78	6
	MOTA	8226		HEP L	1 1	32.042 33.258		25.468	1.00 99.68	6
	MOTA	8227		HEP L	1	34.107	19.901	26.462	1.00 97.90	6
_	MOTA	8228		HEP L	1	33.049	21.220	28.203	1.00 99.77	6
5	MOTA	8229 8230	C6	HEP L	1	32.154	21.953	27.266	1.00101.85	6
	ATOM ATOM	8231	C7	HEP L	ī	34.051	19.067	28.833	1.00 98.50	6
	ATOM	8232	C8	HEP L	1	35.030	19.802	29.773	1.00 97.76	6
	ATOM	8233	04	HEP L	1	34.441	19.860	31.064	1.00 96.20	8
10	MOTA	8234	N1	HEP L	1	32.880	22.043	25.968	1.00103.11	7
. •	ATOM	8235	S1	HEP L	1	31.207	23.336	22.418	1.00113.66	16
	MOTA	8236	01	HEP L	1	31.826	22.878	21.182	1.00113.59	8
	ATOM	8237	02	HEP L	1	31.477	24.685	22.941	1.00111.64 1.00111.51	8 8
	ATOM	8238	03	HEP L	1	29.701	23.322	22.307	1.00 98.16	7
15	MOTA	8239	N2	HEP L	1	33.333	19.839	27.737 24.248	1.00108.88	6
	MOTA	8240	C1	HEP L	2	19.833 20.653	49.708 49.684	25.518	1.00104.63	6
	ATOM	8241	C2	HEP L	2	19.090	47.814	26.172	1.00100.27	6
	MOTA	8242	C3	HEP L	2 2	18.728	46.788	27.241	1.00 98.30	6
20	MOTA	8243	C4 C5	HEP L	2	19.702	48.326	28.859	1.00100.12	6
20	MOTA	8244 8245	C6	HEP L	2	20.022	49.380	27.845	1.00101.78	6
	MOTA MOTA	8245	C7	HEP L	2	18.080	46.646	29.663	1.00 97.02	6
	MOTA	8247	C8	HEP L	2	19.186	46.065	30.550	1.00 96.36	6
	ATOM	8248	04	HEP L	2	19.161	46.714	31.805	1.00 95.77	8
25	ATOM	8249	N1	HEP L	2	20.281	48.676	26.560	1.00102.78	7
	ATOM	8250	S1	HEP L	2	20.640	50.530	22.892	1.00112.59	16
	ATOM	8251	01	HEP L	2	20.348	49.765	21.697	1.00113.24	8 8
	MOTA	8252	02	HEP L	2	22.024	50.791	23.309	1.00111.25	
	ATOM	8253	О3	HEP L	2	20.059	51.924	22.770 28.507	1.00111.32	7
30	MOTA	8254	N2	HEP L	2	18.478	47.544 70.369	23.900	1.00109.55	6
	MOTA	8255	C1	HEP L	3	42.028 42.091	69.312	25.003	1.00104.54	6
	MOTA	8256	C2	HEP L	3 3	40.178	70.594	25.988	1.00 97.17	6
	MOTA	8257 8258	C3 C4	HEP L.	3	39.192	70.688	27.124	1.00 96.78	6
35	ATOM ATOM	8259	C5	HEP L	3	40.844	69.540	28.502	1.00 98.62	6
33	ATOM	8260	C6	HEP L	3	41.854	69.476	27.408	1.00100.28	6
	ATOM	8261	C7	HEP L	3	39.103	70.891	29.639	1.00 97.37	6
	ATOM	8262	C8	HEP L	3	38.600	69.616	30.336	1.00 97.34	6
	ATOM	8263	04	HEP L	3	39.310	69.466	31.552	1.00 95.42	8
40	MOTA	8264	N1	HEP L	3	41.104	69.418	26.123	1.00100.25	7
	MOTA	8265	S1	HEP L	3	42.851		22.390	1.00113.40 1.00112.83	16 8
	MOTA	8266	01	HEP L	3	41.999	70.352	21.301	1.00112.83	8
	MOTA	8267	02	HEP L	3	43.216	68.464 70.580	22.535 22.342	1.00111.22	8
4=	MOTA	8268	03	HEP L	3	44.208 39.982	70.756	28.394	1.00 97.91	7
45	MOTA	8269		HEP L	3 4	67.843	54.529	23.109	1.00109.23	6
	MOTA	8270		HEP L HEP L	4	67.696	54.053	24.549	1.00105.70	6
	MOTA	8271 8272			4	67.448	56.488	25.071	1.00101.29	б
	ATOM ATOM	8272			4	67.199	57.526	26.150		б
50	ATOM	8274			4	68.223	55.960	27.701	1.00100.32	6
00	ATOM	8275			4	68.526	54.948	26.646	1.00101.68	6
	MOTA	8276			4	68.126	58.362	28.296		6
	MOTA	8277			4	67.284		29.528		6
	MOTA	8278				68.179		30.594		8
55	MOTA	8279	N1	HEP L		67.472		25.609		7 16
	MOTA	8280				67.556		21.895 20.813		8
	MOTA	8281				66.829				
	MOTA	8282				67.011		_		
60	ATOM					68.908 68.258				
60						62.836				
	MOTA	8285	י עד	. FLEAT L	, ,	02.050				

	WO 01/5	8951						PCT/EP01/01457			
						-208					
	MOTA	8286	C2	HEP L	5	62,164	25.268	24.495		04.37	6
	ATOM	8287	C3	HEP L	5	64.426	25.352	25.555	1.00		6
	ATOM	8288	C4	HEP L	5	65.270	25.934	26.676	1.00		6
	MOTA	8289	C5	HEP I	. 5	63.215	26.126	27.960	1.00		6
5	MOTA	8290	C6	HEP I	· 5	62.366	25.505	26.903	1.001		6
	MOTA	8291	_ C7	HEP I	, 5	65.381	26.089	29.165	1.00		6
	MOTA	8292	C8	HEP I	, 5	65.085	27.500	29.708	1.00		б
	MOTA	8293	04	HEP I	5	64.379	27.406	30.942	1.00	98.36	8
	MOTA	8294	N1	HEP I	. 5	63.001	25.830	25.594	1.001	_	7
10	MOTA	8295	S1	HEP I	5 د	61.935	24.146	21.985	1.001		16
,	ATOM	8296	01	HEP I	5 ر	62.912	24.120	20.912	1.001	12.36	8
'	ATOM	8297	02	HEP I	5 ر	60.852	25.151	22.006		11.63	8
	ATOM	8298	03	HEP I	5 د	61.166	22.846	22.024		11.95	8
	MOTA	8299	N2	HEP I	5 د	64.610	25.582	27.957	1.00	98.40	7
15	END										
			Ato	m							
				Resid	lue #	<u>x</u>	<u>¥</u>	<u>z</u>	<u>occ</u>	<u>B</u>	

20

Table 1: Structural coordinates of AChBP

"Atom type" refers to the element whoose coordinate are measured. The first letter in the column defines the element.

"Residue" refers to the amino acid in the AChBP protein sequence, using the standard three letter abbreviations known in the art.

"#" refers to the residue number.

"X, Y, Z" crystallographically define the atomic position, in three-dimensional space, of the element measured.

"OCC" is the occupancy volume.

30 "B" is a thermal factor that measures movement of the atom around its atomic center.

PCT/EP01/01457

## -209 Claims

 A water-soluble protein derived from a mollusc being capable of binding a ligand of a ligand-gated receptor.

5

20

35

- 2. The protein of claim 1, wherein the ligand is acetylcholine, gamma-aminobutyric acid (GABA), glycine or serotonin.
- 3. The protein of claim 2, wherein said protein is a acetylcholine-binding protein (AChBP).
  - 4. The protein of any one of claim 1 to 3 which is capable of forming multimers.
- 5. The protein of any one of claims 1 to 4 which is derived form a Pulmonata species, preferably from a Basommatophora species.
  - 6. The protein of any one of claims 1 to 5 comprising an amino acid sequence selected from the group consisting of:
    - (a) an amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4,
       6 or 8 or a functional equivalent thereof, or a fragment of at least 5 continuous amino acids thereof;
    - (b) an amino acid sequence having at least 30% amino acid identity to the amino acid sequence of any one of SEQ ID Nos. 2, 4, 6 or 8.
- A water-soluble ligand binding protein capable of binding a ligand of a ligand-gated receptor and comprising at least 5 continuous amino acids of the aminoacid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8 and/or said protein is detectable by a monoclonal or polyclonal antibody which recognises, preferably with a binding affinity of at least 10⁻⁷M, a protein of any one of claims 1 to 6.
  - 8. A water-soluble protein being capable of binding a ligand of a ligand-gated receptor comprising
    - (a) at least the amino acids of the water-soluble protein of any one of claims 1 to 6 determining solubility of said protein, in the same or corresponding positions as in said protein; and
      - (b) at least 4 amino acids determining binding to said ligand.

PCT/EP01/01457

- -210
- 9. The protein of claim 7 or 8 which is capable of forming multimers.
- 10. The protein of any one of claims 7 to 9 comprising 200-240 amino acids.

5

- 11. The protein of any one of claims 7 to 10, wherein the ligand is acetylcholine, nicotine, lophotoxin, d-tubocurarine, carbamylcholine, galanthamine or epibatidine.
- 10 12. The protein of any one of claims 1 to 11, wherein said ligand-gated receptor is derived from an arthropod (preferably insect), a plant (preferably a higher plant, most preferably a seed plant) or a chordate (preferably a mammalian, most preferably human).
- 15 13. The protein of any one of claims 7 to 12, wherein said ligand-gated receptor is a nicotinic acetylcholine receptor.
- 14. The protein of any one of claims 7 to 13, wherein said amino acids determining solubility are in the same positions as in the AChBP having the amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4, 6 or 8; preferably in which said solubility-determining amino acids comprise solvent accessible regions in the crystal structure according to Figure 10.
- 15. The protein of any one of claims 7 to 14 comprising an amino acid sequence having at least 40% amino acid identity to the amino acid sequence 20-223 of any one of SEQ ID Nos. 2, 4, 6 or 8, in which the ligand binding amino acids have been replaced with the corresponding amino acids of a ligand-gated receptor.
- The protein of any one of claims 7 to 15, in which said solubility-determining amino acids (a) comprise hydrophilic amino acids (Asp, Glu, Arg, Lys) from the sequences 20-44, 73-81, 86-92, 112-120, 135-152, 166-189, 196-20, 209-213, and/or 219-227 of SEQ ID No. 2.
- 35 17. The protein of claim 16, in which said solubility determining amino acids (a) comprise amino acids Asp(36), Asp(68), Glu(115), Arg(137), Asp(143), Asp(148), Glu(150), Arg(167), Arg(189), Glu(215) of SEQ ID No.2, wherein

15

30

-211

PCT/EP01/01457

- Asp may be exchanged for Glu and vice versa and Lys may be exchanged for Arg and vice versa.
- 18. The protein of any one of claims 7 to 17 which further comprises the amino acids Cys(142), Thr(149), Ala(153), Thr(154), Cys(155), Arg(156), Ile(157) and/or Lys(158) of SEQ ID No. 2.
- 19. The protein of any one of claims 7 to 17 which comprises the amino acids (b) Pro(39), Trp(77), Trp(101), Pro(103), Asp(194), and/or Ser(161) of SEQ ID No. 2.
  - 20. The protein of any one of claims 7 to 19 in which the amino acid sequences 165-169 and/or 200-203 of SEQ ID No. 2 have been exchanged with the corresponding sequence of the ligand-gated receptor.
- 21. The protein of any one of claims 7 to 20 which is capable of binding a ligand of an acetylcholine receptor, in which at least one of the amino acid sequences Trp(101) Tyr(T08), Trp(162) His(164) and Tyr(204) Tyr(211) of SEQ ID No. 2 have been exchanged with the corresponding sequence of the acetylcholine receptor.
- 22. A method for the production of a water-soluble ligand-gated receptor or a corresponding ligand-binding domain or for improving the water solubility and accessibility to crystallization of such a receptor or domain, said method comprising altering the amino acid sequence of the extracellular domain of a ligand-gated receptor by way of substituting, adding, deleting or modifying at least one amino acid at a position corresponding to an amino acid determining or contributing to the water-solubility of the protein of any one of claims 1 to 21.
  - 23. The method of claim 22, wherein the ligand-gated receptor is defined as in any one of claims 1 to 21.
- The method of claim 22 or 23, wherein at least one amino acid is altered to the corresponding amino acid of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8, or to a an equivalent amino acid, preferably

10

20

30

WO 01/58951 PCT/EP01/01457

-212

in which said solubility-determining amino acids comprise solvent accessible regions in the crystal structure according to Figure 10.

- The method of any one of claims 22 to 24, wherein loop Cys123-Cys136 of
   SEQ ID No. 2 is inserted into the corresponding region of the ligand binding domain of the ligand-gated receptor.
  - 26. The method of any one of claims 22 to 25 further comprising
  - (a) culturing a host cell transfected with and capable of expressing a polynucleotide comprising a nucleotide sequence encoding the altered amino acid sequence; and optionally
    - (b) recovering said water-soluble ligand-gated receptor or corresponding ligand-binding domain from the culture.
- 15 27. A water-soluble ligand-gated receptor or ligand-binding domain obtainable by the method of any one of claims 22 to 26.
  - 28. The protein of any one of claims 1 to 21 or 27 further comprising a spacer sequence allowing coupling with a carrier body.

29. A fusion protein comprising the water-soluble ligand-binding protein of any one of claims 1 to 21, 27 or 28, or a binding fragment thereof and a fragment of a ligand-gated receptor

- 25 30. A dimer or pentamer consisting of at least one monomer comprising a protein of any one of claims 1 to 21 or 27 to 29.
  - 31. A ligand-gated ion channel comprising a protein of any one of claims 1 to 21 or 27 to 29 or the dimer or pentamer of claim 30.
  - 32. One or more polynucleotides encoding the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31.
- 35 33. The polynucleotide(s) of claim 32 which comprise(s)

WO 01/58951 PCT/EP01/01457

-213

- (a) a nucleotide sequence having at least 15 continuous nucleotides of the nucleotide sequence depicted in any one of SEQ ID Nos. 1, 3, 5 or 7 or a degenerated sequence thereof; or
- (b) a nucleotide sequence capable of hybridizing to a nucleotide sequence of (a) under stringent hybridisation conditions.
- 34. The polynucleotide(s) of claim 32 or 33 which is(are) operatively linked to heterologous expression control sequences allowing expression inprokaryotic or eukaryotic cells.

10

5

- 35. One or more vector(s) containing the polynucleotide(s) of any one of claims 32 to 34.
- 36. A host cell genetically engineered with the polynucleotide(s) of any one claims
  32 to 34 or with the vector(s) of claim 35.
  - 37. An antigen comprising an epitope of at least 5 continuous amino acids of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8 and/or said epitope is detectable by a monoclonal or polyclonal antibody which recognises, preferably with a binding affinity of at least 10⁻⁷M, a protein of any one of claims 1 to 6.
- 38. An antibody specifically recognizing the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31 or the antigen of claim 37.
  - 39. An oligonucleotide probe comprising a nucleotide sequence having at least 15 continuous nucleotides of a polynucleotide of any one claims 32 to 34 or encoding the antigen of claim 37.

30

35

20

40. A composition comprising the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31, the polynucleotide(s) of any one claims 32 to 34, the vector(s) of claim 35, the host cell of claim 36, the antigen of claim 37, the antibody of claim 38, or an oligonucleotide probe of claim 39; and optionally suitable means for detection or performing a ligand-receptor binding assay.

PCT/EP01/01457

-214

41. A method for identifying an agonist/activator or antagonist/inhibitor of a ligandgated receptor comprising the steps of:

- (a) contacting the water-soluble ligand-binding protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31 or a cell expressing said protein in the presence of components capable of providing a detectable signal in response to ligand binding with a compound to be screened under conditions that permit binding of said compound to the ligand-binding protein; and
- 10 (b) detecting the presence or absence of a signal generated from the binding activity of the ligand-binding protein, wherein the presence/increase and absence/decrease of the signal is indicative for an agonist/activator and antagonist/inhibitor, respectively, of a ligand-gated receptor.

15

5

WO 01/58951

- 42. A crystal of a protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31.
- 43. A crystal of a protein-ligand complex comprising a protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31; and a ligand.
  - 44. The crystal of claim 43, wherein the ligand comprises an N-alkylated hydroxyalkyl and/or a quaternary ammonium ion.

25

The crystal of claim 43, wherein the ligand comprises 4-(2-Hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), B-bippinatin, lophotoxin, d-tubocurarine, carbamylcholine, galanthamine, epibatidine or alphabungarotoxin.

30

46. The crystal of any one of claims 42 to 45, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein or protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms.

35

47. The crystal of any one claims 42 to 46, wherein the protein has an amino acid sequence of amino acids 20 to 223 of SEQ ID No. 2, or an amino acid

WO 01/58951 PCT/EP01/01457

-215

sequence that differs from amino acid 20 to 223 of SEQ ID No. 2 by only having conservative substitutions.

48. The crystal of claim 47, wherein the ligand is HEPES.

5

- 49. The crystal of claim 46 having (1) a space group of P2₁2₁2₁ and a unit cell of dimensions of a=120.6Å, b=137.0Å and c=161.5Å; (2) a space group of P4₂2₁2 and a unit cell of dimensions of a=b=141.6Å and c=120.8Å or (3) a space group of P2₁ and a unit cell of dimensions of a=121.1Å, b=162.1Å, c=139.4Å, β=90.1°.
- 50. The crystal of any one of claims 42 to 49, wherein the protein has secondary structural elements that include .alpha.-helix and antiparallel .beta.-sheets as shown in Figure 7, 10, 11 and/or 12.

15

25

30

10

- 51. The crystal of any one claims 42 to 50 having a three-dimensional structure as defined by atomic coordinates shown in Table 1.
- 52. The crystal of any one of claims 42 to 51 having a binding cavity as shown in Figure 6, 8, 9 and/or 13.
  - 53. A method of using the crystal of any one of claims 42 to 52 in a drug screening assay comprising:
    - selecting a potential ligand by performing structure assisted drug
      design with the three-dimensional structure determined for the crystal,
      wherein said selecting is performed in conjunction with computer
      modeling; optionally
    - (b) contacting the potential ligand with the ligand binding domain of the ligand-gated receptor in an in vitro or in vivo assay; and
    - (c) detecting the binding of the potential ligand for the ligand binding domain.
  - 54. The method of claim 53, wherein the ligand-gated receptor is a nicotinic acetylcholine receptor.

35

55. The method of claim 53 or 54 further comprising:

WO 01/58951 PCT/EP01/01457 -216

- (d) forming a supplemental crystal of a protein-ligand complex by cocrystallization or soaking the crystal of the water-soluble ligand-binding protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31, with a potential drug, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms, more preferably greater than 3;
- (e) determining the three-dimensional structure of the supplemental crystal;
- (f) selecting a candidate drug by performing a structure assisted drug design with the three-dimensional structure determined for the supplemental crystal, wherein said selecting is performed in conjunction with computer modeling; optionally
- (g) contacting the candidate drug with a cell that expresses the ligandgated receptor; and
- (h) detecting a cell response; wherein a candidate drug is identified as a drug when the cell response is altered compared to a cell that has not been contacted with the candidate compound.

20

25

15

5

10

56. The method of any one of claims 53 to 55 further comprising an initial step that precedes step (a) wherein said initial step consists of determining the three-dimensional structure of a crystal comprising a protein-ligand complex formed between the water-soluble ligand-binding protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31, and the ligand of the ligand-gated receptor, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms.

30

35

- 57. A method of growing a crystal of a protein-ligand complex comprising:
  - (a) contacting the water-soluble ligand-binding protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31 with a ligand of a ligand-gated receptor, wherein the water-soluble ligand-binding protein forms a protein-ligand complex with the ligand; and

WO 01/58951

PCT/EP01/01457

-217

(b) growing the crystal of the protein-ligand complex; wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms.

5

- 58. A drug screening assay comprising soaking the crystal of any one of claims 42 to 52 in a solution of compounds to be screened and detecting the binding of the compound to the ligand-binding protein.
- 10 59. The method of claim 57 or 58, wherein said ligand comprises an alkylated nitrogen and/or quaternary ammonium ion.
  - 60. A method of increasing or decreasing the affinity of a drug to a ligand-gated receptor, comprising
- 15 performing structure assisted drug design with the three-dimensional (a) structure determined for the crystal of any one of claims 42 to 52, wherein said drug design is performed in conjunction with computer modeling; and

(b) modifying said drug to alter or eliminate a portion thereof suspected of Interacting with a binding site of the binding cavity or

with a non-specific binding site of the protein in the crystal.

61. The method of claim 60, wherein step (a) further comprises the steps of a method of any one of claims 53 to 59.

25

20

- 62. The method of claim 60 or 61, further comprising after step (b), the additional step of:
  - repeating the method used to perform structure assisted drug design (c) according to step (a) using the modified drug according to step (b).

30

35

63. A method of drug design comprising the step of using the structural coordinates of a water-soluble ligand-binding protein crystal comprising the coordinates of Table 1, to computationally evaluate a chemical entity for associating with the ligand-binding site or a non-specific binding site of a ligand-binding protein.

WO 01/58951

30

PCT/EP01/01457

-218

- 64. The method of any one of claims 53 to 63, wherein the identified drug prevents or promotes correct assembly of a ligand-gated ion channel.
- 65. The method of any one of claims 53 to 63, wherein the identified drug binds to a non-specific binding site of a ligand-gated ion channel.
  - 66. The method of any one of claims 53 to 65 further comprising synthesizing the drug in a therapeutically effective amount.
- 10 67. A drug produced by the method of claim 66 or a pro-drug thereof.
- 68. The drug of claim 67 which interacts with a ligand-gated receptor comprising a pentamer of claim 30 with monomers A to E, wherein the drug binds to one or more primary contact regions of a monomer (residues from A contacting B) defined by amino acid residues 15 to 21, 44 to 47, 85 to 87, 91 to 94, 122 to 124, 143 to 146, 149, 185 to 187 of the mature protein of SEQ ID No. 2 and/or to one or more of the complementary contact regions of the other monomer (from B contacting A, (identical to residues on A contacting E) defined by amino acid residues 3 to 4, 7 to 8, 11, 37 to 39, 53, 75 to 77, 96 to 104, 114 to 118 and 163-170 of the mature protein of SEQ ID No. 2; or to the contact regions as identified in Figure 14; or to the corresponding contact regions of the monomers of a ligand-gated ion channel.
- The drug of claim 68, wherein the ligand-gated ion channel is the nicotinic
   acetylcholine receptor and the order of the monomers is αγαβδ.
  - 70. A computer readable medium comprising a nucleotide sequence of the polynucleotide(s) of any one of claims 32 to 34, an amino acid sequence of a protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31, or the structural coordinates of a crystal of any one of claims 40 to 50.
  - 71. A device comprising the computer readable medium of claim 70.
- 35 72. Use of the computer readable medium of claim 70 or the device of claim 71 for modeling an antagonist/inhibitor or agonist/activator of a ligand-gated receptor.

WO 01/58951 PCT/EP01/01457

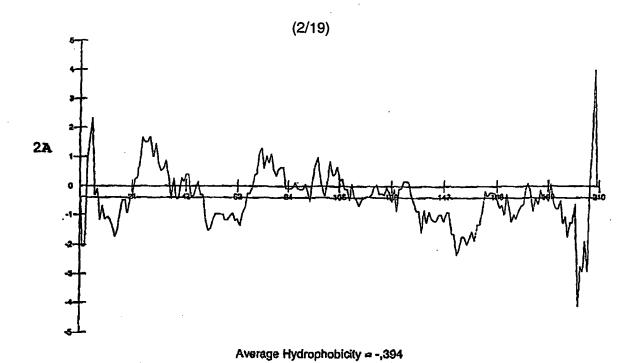
-219

- 73. Use of the crystal of any one of claims 42 to 52 or its structural coordinates as a template for modeling the 3D structure of a ligand-gated ion channel.
- 5 74. Use of the polynucleotide(s) of any one of claims 32 to 34, the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31, the vector(s) of claim 35, the host cell of claim 36, the antigen of claim 37, the antibody of claim 38, an oligonucleotide probe of claim 39, the crystal of any one of claims 42 to 52 or a method of any one of claims 53 to 66 for screening or profiling putative ligands of ligand-gated receptors.
- Use of an antagonist/inhibitor or agonist/activator identified according to a method of any one of claims 53 to 66 for the preparation of a pharmaceutical composition for the treatment of a ligand-gated ion channel mediated or related disorder.
- 76. The use of claim 75, wherein the antagonist/inhibitor is or is derived from the protein of any one of claims 1 to 21 or 27 to 29, an antigen of claim 37, an antibody of claim 38 or from a toxin of the ligand-gated ion channel.
- 77. The use of claim 75, wherein the agonist/activator is or is derived from a the protein of any one of claims 1 to 21 or 27 to 29, an antigen of claim 37, an antibody of claim 38 or from epibatidine, acetylcholine, choline, nicotine, carbachol, serotonin or GABA.
- 78. The use of any one claims 75 to 77, wherein the ligand-gated ion channel is the nicotinic acetylcholine receptor and said mediated or related disorder is Tourette's syndrome, Alzheimer's disease, addiction to nicotine or schizophrenia.
  - 79. Use of ligand of a ligand-gated receptor for identifying and isolating a water-soluble ligand-binding protein from a mollusc.
- 35 80. The use of claim 79, wherein said ligand is  $\alpha$ -bungarotoxin.

## (1/19)

L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	MRRNIFCLACLWIVQACLSLDRADILYNIRQTSRPDVIPTQRDRPVAVSVSLKFINILMRRNIFCLACLWIVQGCLSLDRADILYNIRQTSRPDVIPTQRDRPVAVSVSLKFINIL MAELRRIILLLCTIAFHVSHGQIRWTLLNQITGESDVIPLSNNTPLNVSLNFKLMNIV MAELRGIILLLCTIAFHVSHGQIRWTLLNQITGESDVIPLSNNTPLNVSLNFKLMNIL  * *: * * .: * ;* ;* * * * * * * * * * * * * * *
L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	EVNEITNEVDVVFWQQTTWSDRTLA-WNSSHSPDQVSVPISSLWVPDLAAYNAISKPEVL EVNEITNEVDVVFWQQTTWSDRTLA-WNSSHSPDQVSVPISSLWVPDLAAYNAISKPEVL EADTEKDQVEVVLWTQASWKVPYYSSLLSSSSLDQVSLPVSKMWTPDLSFYNAIAAPELL EADTEKDQVEVVLWTQASWKVPYYSSLLSSSSLDQVSLPASKMWTPDLSFYNAIAAPELL *.: .::*:**: *:: : : * * * * * * * * * *
L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	TPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESGATCRIKIGSWTHHSREISVDPTTE- TPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESGATCRIKIGSWTHHSGEISVDPTTE- SADRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPGATCRIKVGSWTHDNKQFALITGEEG STDRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPGATCRIKVGSWTFDNKQLALITGEEG : * .**.*:** * **:**: .*************
L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	NSDDSEYFSQYSRFEILDVTQKKNSVTYSCCPEAYEDVEVSLNFRKKGRSEIL NSDDSEYFSQYSRFEILDVTQKKNSVIYSCCPEAYEDVEVSLNFRKKGRSEIL VVNIAEYFDS-PKFDLLSATQSLNRKKYSCCENMYDDIEITFAFRKK VVNIAEYFDS-PKYDLLSATQSLNRKKYRCCENMYEDIEITFAFRKK : :***:::*** * * * * : *:*::: ****

Figure 1



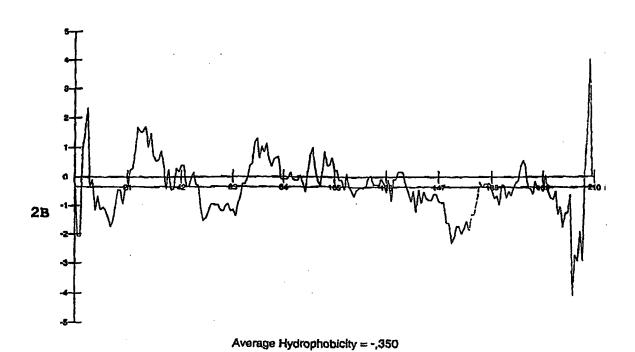
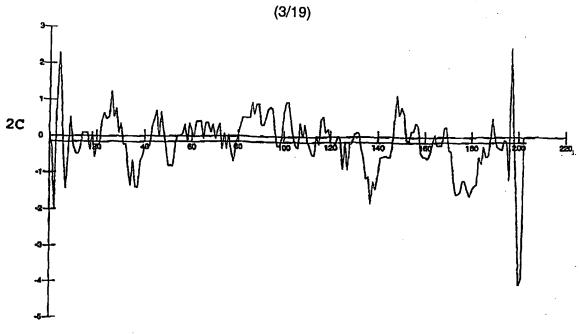


Figure 2



Average Hydrophobicity = -,159

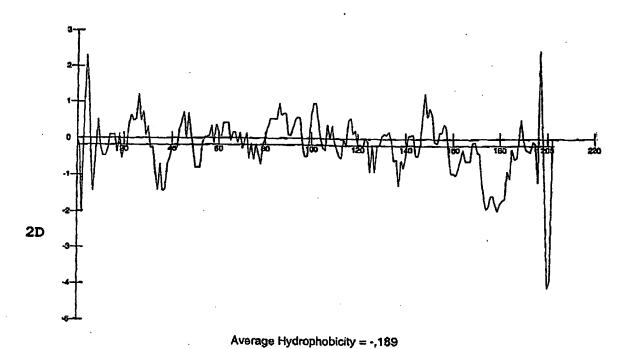


Figure 2 (continued)

## (4/19)

L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	QRDR-PVAVSVSLKFINILEVNEITNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPI QRDR-PVAVSVSLKFINILEVNEITNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPI SNNT-PLNVSLNFKLMNIVEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPV SNNT-PLNVSLNFKLMNILEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPA ANDSQPLTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTVRFPD RDWRKPTTVSIDVIVYAILNVDEKNQVLTTYIWYRQYWTDEFLQWNPEDFDNITKLSIPT FKGP-PVNVSCNIFINSFGSIAETTMDYRVNIFLRQQWNDPRLAYNEYPDDSLDLDPSML LGER-VTEVKTDIFVTSFGPVSDHDMEYTIDVFFRQSWKDERLKF-KGPMTVLRLNNLMA
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	SSLWVPDLAAYNAISK-PEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSG-VDTESGA SSLWVPDLAAYNAISK-PEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSG-VDTESGA SKMWTPDLSFYNAIAA-PELLSADRVVVSKDGSVIYVPSQRVRFTCDLIN-VDTEPGA SKMWTPDLSFYNAIAA-PELLSTDRVVVSKDGSVIYVPSQRVRFTCDLIN-VDTEPGA GQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQYLPPGIFKSSCYIDVRWFPFDVQ DSIWVPDILINEFVDV-GKSPNIPYVYIRHQGEVQNYKPLQVVTACSLDIYNFPFDVQ DSIWKPDLFFANEKGAHFHEITTDNKLLRISRNGNVLYSIRITLTLACPMDLKNFPMDVQ SKIRTPDTFFHNGKKSVAHNMTMPNKLLRITEDGTLLYTMRLTVRAECPMHLEDFPMDAH: ** : * : * : * : * : * : * * : * * : * * : * * * : * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	TCRIKIGSWTHHSREISVDPTTE-NSDDSEYFSQYSRFEILDVTQKKNSVTYSCCPE TCRIKIGSWTHHSGEISVDPTTE-NSDDSEYFSQYSRFEILDVTQKKNSVIYSCCPE TCRIKVGSWTHDNKQFALITGEEGVVNIAEYFDS-PKFDLLSATQSLNRKKYSCCEN TCRIKVGSWTFDNKQLALITGEEGVVNIAEYFDS-PKYDLLSATQSLNRKKYRCCEN HCKLKFGSWSYGGWSLDLQMQEADISGYIPN-GEWDLVGIPGKRSERFYECCKE NCSLTFTSWLHTIQDINISLWRLPEKVKSDRSVFMNQ-GEWELLGVLPYFREFSMESS-N TCIMQLESFGYTMNDLIFEWQEQGAVQVADGLTL-PQFILKEEKDLRYCTKHYNT-G ACPLKFGSYAYTRAEVVYEWTR-EPARSVVVAEDGSRLNQYDLLGQTVDSGIVQSSTG *: *:
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	AYEDVEVSLNFRKKGRSEIL AYEDVEVSLNFRKKGRSEIL MYDDIEITFAFRKK MYEDIEITFAFRKK PYPDVTFTVTMRRRTLYYGL YYAEMKFYVVIRRPLFYVV KFTCIEARFHLERQMGYYLI EYVVMTTHFHLKRKIGYFVI : : :::

Figure 3

## (5/19)

nAChR_h-A2	MGPSCPVFLSFTKLSLWWLLLTPAGGEEAKRPPPRAPGDPLSSPSPTALPQGGSHTE
nAChR_h-A4	PLLLLLGTGLLRASSHVE
nAChR_h-A5	MAARGSGPRALRLLLLVQLVAGRCGLAGAAGGAQRGLSEPS
nAChR_h-A3	LLLSLLPVARASE
nAChR_h-A6	WICVFTPFFKCCVCCA
nAChR_h-A1	EFSLCSAGLVI.GSE
nAChR_h-A7	LHVSLOG-EFOR
nAChR_h-A9	AAETADG-KYAO
B-AChBP_T1	IAFHVSHG-OIR
B-AChBP_T2	TAFHVSHG-OIR
L-AChBP T1	wivoacls-ldr
L-AChBP_T2	WIVQGCLS-LDR
	·
nAChR_h-A2	TEDRLFKHLFRGYNRWARPVPNTSDVVIVRFGLSIAQLIDVDEKNQMMTTNVWLKQ
nAChR_h-A4	TRAHAEERLLKKLFSGYNKWSRPVANISDVVLVRFGLSIAQLIDVDEKNQMMTTNVWVKQ
nAChR_h-A5	SIAKHEDSLLKDLFQDYERWVRPVEHLNDKIKIKFGLAISQLVDVDEKNQLMTTNVWLKQ
nAChR_h-A3	AEHRLFERLFEDYNEIIRPVANVSDPVIIHFEVSMSQLVKVDEVNQIMETNLWLKQ
nAChR h-A6	TEERLFHKLFSHYNQFIRPVENVSDPVTVHFEVAITQLANVDEVNQIMETNLWLRH
nAChR h-A1	HETRLVAKLFKDYSSVVRPVEDHRQVVEVTVGLQLIQLINVDEVNQIVTTNVRLKQ
nAChR h-A7	KLYKELVKNYNPLERPVANDSQPLTVYFSLSLLQIMDVDEKNQVLTTNIWLQM
nAChR h-A9	KLFNDLFEDYSNALRPVEDTDKVLNVTLQITLSQIKDMDERNQILTAYLWIRQ
B-AChBP T1	WTLLNQITGESDVIPLSN-NTPLNVSLNFKLMNIVEADTEKDQVEVVLWTQA
B-AChBP T2	WTLLNQITGESDVIPLSN-NTPLNVSLNFKLMNILEADTEKDQVEVVLWTQA
L-AChBP T1	ADILYNIRQTSRPDVIPTQR-DRPVAVSVSLKFINILEVNEITNEVDVVFWQQT
L-ACHBP T2	ADILYNIRQTSRPDVIPTQR-DRPVAVSVSLKFINILEVNEITNEVDVVFWQQT
_	*
nAChR h-A2	EWSDYKLRWNPTDFGNITSLRVPSEMIWIPDIVLYNNADGEFAVTHMTKAHLFSTGTVHW
nAChR h-A4	EWHDYKLRWDPADYENVTSIRIPSELIWRPDIVLYNNADGDFAVTHLTKAHLFHDGRVQW
nAChR h-A5	EWIDVKLRWNPDDYGGIKVIRVPSDSVWTPDIVLFDNADGRFEGTS-TKTVIRYNGTVTW
nAChR h-A3	IWNDYKLKWNPSDYGGAEFMRVPAQKIWKPDIVLYNNAVGDFQVDDKTKALLKYTGEVTW
nAChR h-A6	IWNDYKLRWDPMEYDGIETLRVPADKIWKPDIVLYNNAVGDFQVEGKTKALLKYNGMITW
nAChR h-A1	QWVDYNLKWNPDDYGGVKKIHIPSEKIWRPDLVLYNNADGDFAIVKFTKVLLQYTGHITW
nAChR h-A7	SWTDHYLQWNVSEYPGVKTVRFPDGQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQY
nAChR h-A9	IWHDAYLTWDRDQYDGLDSIRIPSDLVWRPDIVLYNKADDESSEPVNTNVVLRYDGLITW
B-AChBP T1	SWKVPYYSS-LLSSSSLDQVSLPVSKMWTPDLSFYN-AIAAPELLSADRVVVSKDGSVIY
B-AChBP T2	SWKVPYYSS-LLSSSSLDQVSLPASKMWTPDLSFYN-AIAAPELLSTDRVVVSKDGSVIY
L-AChBP T1	TWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AISKPEVLTPQLARVVSDGEVLY
L-AChBP T2	TWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AISKPEVLTPQLARVVSDGEVLY
	a de la dela de
nAChR h-A2	VPPAIYKSSCSIDVTFFPFDQQNCKMKFGSWTYDKAKIDLEQMEQ-TVDLKDYWES-GEW
nAChR h-A4	TPPAIYKSSCSIDVTFFPFDQQNCTMKFGSWTYDKAKIDLVNMHS-RVDQLDFWES-GEW
nAChR h-A5	TPPANYKSSCTIDVTFFPFDLQNCSMKFGSWTYDGSQVDIILEDQ-DVDKRDFFDN-GEW
nAChR h-A3	IPPAIFKSSCKIDVTYFPFDYQNCTMKFGSWSYDKAKIDLVLIGS-SMNLKDYWES-GEW
nAChR h-A6	TPPAIFKSSCPMDITFFPFDHQNCSLKFGSWTYDKAEIDLLIIGS-KVDMNDFWEN-SEW
nAChR h-A1	TPPAIFKSYCEIIVTHFPFDEQNCSMKLGTWTYDGSVVAINPESD-QPDLSNFMES-GEW
nAChR h-A7	LPPGIFKSSCYIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQ-EADISGYIPN-GEW
nAChR h-A9	DAPAITKSSCVVDVTYFPFDNQQCNLTFGSWTYNGNQVDIFNALD-SGDLSDFIED-VEW
B-AChBP T1	VPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTHDNKQFALITGEEGVVNIAEYFDS-PKF
B-AChBP T2	VPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTHDNKQFALITGEEGVVNIAEYFDS-PKF VPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTFDNKQLALITGEEGVVNIAEYFDS-PKY
L-AChBP T1	MPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSREISVDPTTE-NSDDSEYFSQYSRF
L-AChBP_T2	MPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSGEISVDPTTE-NSDDSEYFSQYSRF
	a de la companya de l

Figure 4

#### (6/19)

nAChR_h-A2	AIVNATGTYNSKKYDCCAE-IYPDVTYAFVIRRLPLFYTINLIIPCLLISCLTVLVFYLP
nAChR_h-A4	VIVDAVGTYNTRKYECCAE-IYPDITYAFVIRRLPLFYTTNI.TTPCI.T.TCC.TVI.VEVT.P
nAChR_h-A5	EIVSATGSKGNRTDSCCWYPYVTYSFVIKRLPLFYTIFT.TIPCIGISFITVIVEVID
nAChR_h-A3	AIIKAPGYKHDIKYNCCEE-IYPDITYSLYIRRLPLFYTTNI.TPCLI.TSFLTVLVFYLD
nAChR_h-A6	EIIDASGYKHDIKYNCCEE-IYTDITYSFYIRRLPMFYTTNI.TIPCI.FISFI.TVI.VEVI.B
nAChR_h-A1	VIKESRGWKHSVTYSCCPDTPYLDITYHFVMORLPLYFIVNVIIPCLLFSFLTGLVEVLD
nAChR h-A7	DLVGIPGKRSERFYECCKE-PYPDVTFTVTMRRRTI.YYGI.NI.I.TPCVI.TSAIAIIVEITB
nAChR_h-A9	EVHGMPAVKNVISYGCCSE-PYPDVTFTLLLKRRSSFYIVNLLIPCVLISFLAPLSFYLP
B-AChBP_T1	DLLSATQSLNRKKYSCCEN-MYDDIEITFAFRKK
B-AChBP_T2	DLLSATQSLNRKKYRCCEN-MYEDIEITFAFRKK
L-AChBP_T1	EILDVTQKKNSVTYSCCPE-AYEDVEVSLNFRKKGRSEIL
L-AChBP_T2	EILDVTQKKNSVIYSCCPE-AYEDVEVSLNFRKKGRSEIL
_	** * : . :::
nAChR h-A2	SDCGEKITLCISVLLSLTVFLLLITEIIPSTSLVIPLIGEYLLFTMIFVTLSIVITVFVL
nAChR h-A4	SECGEKITLCISVLLSLTVFLLLITEIIPSTSLVIPLIGEYLLFTMIFVTLSIVITVFVL
nAChR h-A5	SNEGEKICLCTSVLVSLTVFLLVIEEIIPSSSKVIPLIGEYLVFTMIFVTLSIMVTVFAI
nAChR h-A3	SDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVIPLIGEYLLFTMIFVTLSIVITVFVL
nAChR h-A6	SDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVVPLVGEYLLFTMIFVTLSIVVTVFVL
nAChR h-A1	TDSGEKMTLSISVLLSLTVFLLVIVELIPSTSSAVPLIGKYMLFTMVFVIASIIITVIVI
nAChR h-A7	ADSGEKISLGITVLLSLTVFMLLVAEIMPATSDSVPLIAQYFASTMIIVGLSVVVTVIVL
nAChR h-A9	AASGEKVSLGVTILLAMTVFQLMVAEIMP-ASENVPLIGKYYIATMALITASTALTIMVM
B-AChBP T1	MAMILTANI WANDALI LINING AND
B-AChBP_T2	
L-AChBP T1	
L-AChBP_T2	
_	
nAChR h-A2	NVHHRSPSTH-TMPHWVRGALLGCVPRWLLMNRP
nAChR h-A4	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE
nAChR h-A5	NIHHRSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR h-A3	NVHYRTPTTH-TMPSWVKTVFLNLLPRVMFMTRP
nAChR_h-A6	NIHYRTPTTH-TMPRWVKTVFLKLLPQVLLMRWP
nAChR h-A1	NTHHRSPSTH-VMPNWVRKVFIDTIPNIMFFSTMK
nAChR h-A7	OVHHHUDDCC-RMDRAMARALDITLI MICCARLE DAND DO
nAChR h-A9	QYHHHDPDGG-KMPKWTRVILLNWCAWFLRMKRPGNIHFCGAEAR-PVPHWARVVILKYMSRVLFVYDVG
B-AChBP T1	THE CORDAN I VERNARY VILKIMSKYLEVIDYG
B-AChBP T2	
L-AChBP T1	
L-AChBP_T2	
nAChR h-A2	VDAEEREVVVEEE
nAChR h-A4	PEGEPPATSGTQSLHPPSPSFCVPLDVPAEPGPSCKSPSDQLPPQQPLEAEKASPHPSPG
nAChR h-A5	TOTAL
nAChR h-A3	TSNEGNAQKPRPLYGAELSNLNCFSRAESKGCKEGYPCQ
nAChR h-A6	PAKGKLASHGEPRH
nAChR_h-A1	PAKGKLASHGEPRH
nAChR h-A7	QDKKQDKKQDKK
nAChR h-A9	
B-AChBP T1	HLTKVYSKLPESN
B-AChBP T2	
L-AChBP T1	
L-AChBP T2	

Figure 4 (continued)

# (7/19)

nAChR_h-A2	DRWACAGHVAPSVGTLCSHGHLHSGASGPKA
nAChR_h-A4	PCRPPHGTQAPGLAKARSLSVQHMSSPGEAVEGGVRCRSRSIQYCVPRDDAAPEADGQAA
nAChR_h-A5	
nAChR_h-A3	DGMCGYCHHRRIKISNFSANLTRSSSSESVDA
nAChR_h-A6	LKECFHCHKSNELATSKRRLSHQPLQW
nAChR_h-A1	KPGPPP
nAChR_h-A7	GNLLYIGFRGLDGVHCVPTPDSGVVCGRMACSPTHD
nAChR_h-A9	LKAARNKDLSRKKDMNKRLKNDLGCOGKNP
B-AChBP_T1	
B-AChBP_T2	
L-AChBP_T1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
L-AChBP_T2	
**************************************	nat t on
nAChR_h-A2	EALLQEGELLLSPHMQKA
nAChR_h-A4	GALASRNTHSAELPPPDQPSPCKCTCKKEPSSVSPSATVKTRSTKAPPPHLPLSPALTRA
nAChR_h-A5	SRNTLEAA
nAChR_h-A3	VLSLSALSPEIKEA
nAChR_h-A6	VVENSEHSPEVEDV
nAChR_h-A1	MGFHSPLIKHPEVKSA
nAChR_h-A7	EHLLHGGQPPEGDPDLAKI
nAChR_h-A9	OEAESYCROUDUIT
B-AChBP_T1	
B-AChBP_T2	
L-AChBP_T1	
L-AChBP_T2	
nAChR h-A2	I ECUIVIADUI DEBDADGGUUDDITANIA
nAChR h-A4	LEGVHYIADHLRSEDADSSVKEDWKYVAMVIDRIFLWLFIIVCFLGTIGLFLPPFLA
_	VEGVQYIADHLKAEDTDFSVKEDWKYVAMVIDRIFLWMFIIVCLLGTVGLFLPPWLA
nAChR_h-A5	LDSIRYITRHIMKENDVREVVEDWKFIAQVLDRMFLWTFLFVSIVGSLGLFVPVIYKWAN
nAChR_h-A3	IQSVKYIAENMKAQNEAKEIQDDWKYVAMVIDRIFLWVFTLVCILGTAGLFLQPLMA
nAChR_h-A6	INSVQFIAENMKSHNETKEVEDDWKYVAMVVDRVFLWVFIIVCVFGTAGLFLQPLLG
nAChR_h-A1	IEGIKYIAETMKSDQESNNAAAEWKYVAMVMDHILLGVFMLVCIIGTLAVFAGRLIE
nAChR_h-A7	LEEVRYIANRFRCQDESEAVCSEWKFAACVVDRLCLMAFSVFTIICTIGILMSAP-NFVE
nAChR_h-A9	TRNIEYIAKCLKDHKATNSKGSEWKKVAKVIDRFFMWIFFIMVFVMTILIIA
B-AChBP_T1	
B-AChBP_T2	
L-AChBP_T1	
L-AChBP_T2	
nAChR h-A2	GMI
nAChR h-A4	GMI
nAChR h-A5	ILIPVHIGNANK
nAChR h-A3	REDA
nAChR h-A6	NTGKS
nAChR_h-A1	
nAChR_h-A7	LNQQG AVSKDFA
nAChR_n-A7	
B-AChBP_T1	
B-AChBP_T2	**************************************
L-AChBP_T1 L-AChBP_T2	
D-WOURE_IZ	
	•

Figure 4 (continued)

#### (8/19)

B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	-MAELRRIILLLCTIAFHVSHG-QIRWTLLNQITGESDVIPLSNNT-PLNVSLNFKLM -MAELRGIILLLCTIAFHVSHG-QIRWTLLNQITGESDVIPLSNNT-PLNVSLNFKLMMRRNIFCLACLWIVQACLS-LDRADILYNIRQTSRPDVIPTQRDR-PVAVSVSLKFIMRRNIFCLACLWIVQGCLS-LDRADILYNIRQTSRPDVIPTQRDR-PVAVSVSLKFIMEPWPLLLLFSLCSAGLVLGSEHETRLVAKLFKDYSSVVRPVEDHRQVVEVTVGLQLI MRCSPGGVWLGLAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQPLTVYFSLSLL : . : * . : : * : : * : *
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	NI VEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPVSKMWTPDLSFYN-AIA NI LEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPASKMWTPDLSFYN-AIA NI LEVNEI TNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AIS NI LEVNEI TNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AIS QLINVDEVNQIVTTNVRLKQQWVDYNLKWNPDDYGGVKKIHI PSEKIWRPDLVLYNNADG QIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTVRFPDGQIWKPDILLYNSADE ::::::::::::::::::::::::::::::::::::
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	APELLSADRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTHDNKQFAL APELLSTDRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTHDNKQLAL KPEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSREISV KPEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSGEISV DFAIVKFTKVLLQYTGHITWTPPAIFKSYCEIIVTHFPFDEQNCSMKLGTWTYDGSVVAI RFDATFHTNVLVNSSGHCQYLPPGIFKSSCYIDVRWFPFDVQHCKLKFGSWSYGGWSL .: * : * : * : * : * : * : * : * : * : *
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	ITGEEGVVNIAEYFDS-PKFDLLSATQSLNRKKYSCC-ENMYDDIEITFAFRKK ITGEEGVVNIAEYFDS-PKYDLLSATQSLNRKKYRCC-ENMYEDIEITFAFRKK DFTTE-NSDDSEYFSQYSRFEILDVTQKKNSVTYSCC-PEAYEDVEVSLNFRKKGRSEIL DFTTE-NSDDSEYFSQYSRFEILDVTQKKNSVIYSCC-PEAYEDVEVSLNFRKKGRSEIL NPESD-QPDLSNFMES-GEWVIKESRGWKHSVTYSCCPDTPYLDITYHFVMQRLPLYFIV DLQMQ-EADISGYIPN-GEWDLVGIPGKRSERFYECC-KEPYPDVTFTVTMRRRTLYYGL : ::::.::
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	NVIIPCLLFSFLTGLVFYLPTDSGEKMTLSISVLLSLTVFLLVIVELIPSTSSAVPLIGK NLLIPCVLISALALLVFLLPADSGEKISLGITVLLSLTVFMLLVAEIMPATSDSVPLIAQ
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	YMLFTMVFVIASIIITVIVINTHHRSPSTHVMPNWVRKVFIDTIPNIMFFSTMKRPSREK YFASTMIIVGLSVVVTVIVLQYHHHDPDGGKMPKWTRVILLNWCAWFLRMKRPGEDK
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	QPPMGVRPACQHKQRRCSLASVEMSAVGPPPASNGNLLYIGFRGLDGVHCVPTPDSGVVCGRMAC

#### (9/19)

B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	FHSPLIKHPEVKSAIEGIKYIAETMKSDQESNNAAAEWKYVAMVMDHILL SPTHDEHLLHGGQPPEGDPDLAKILEEVRYIANRFRCQDESEAVCSEWKFAACVVDRLCL
B-AChBP T1.	
B-AChBP T2.	
L-AChBP_T1.	
L-AChBP_T2.	
A1_human	GVFMLVCIIGTLAVFAGRLIELNQQG
A7_human	MAFSVFTIICTIGILMSAPNFVEAVSKDFAZ

Figure 5 (continued)

(10/19)

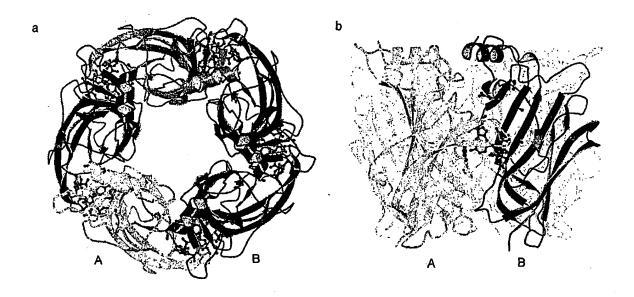
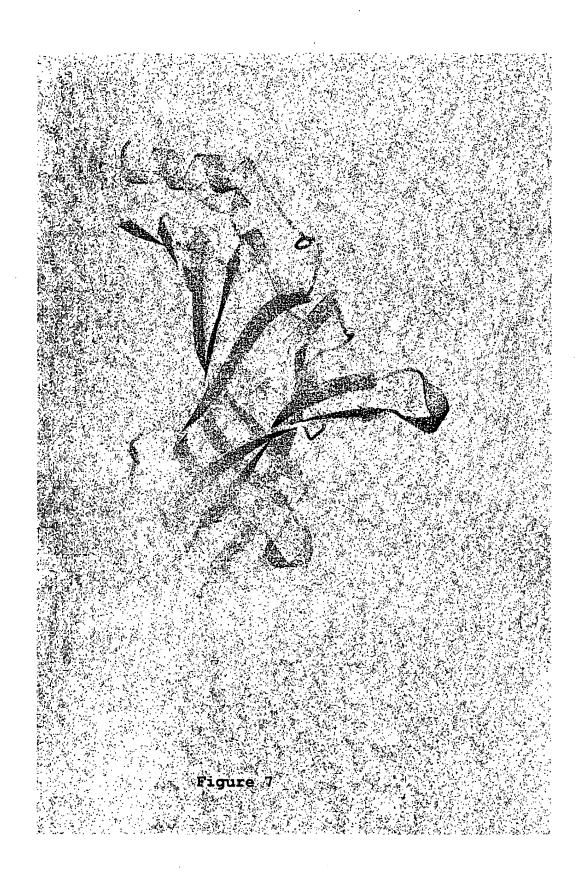
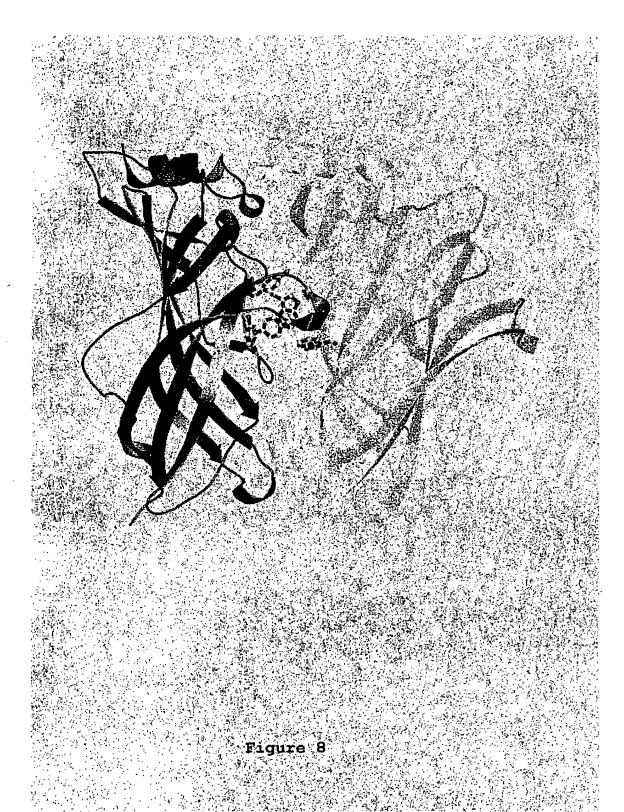


Figure 6

(11/19)



(12/19)



(13/19)

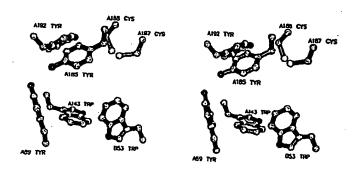


Figure 9

(14/19)

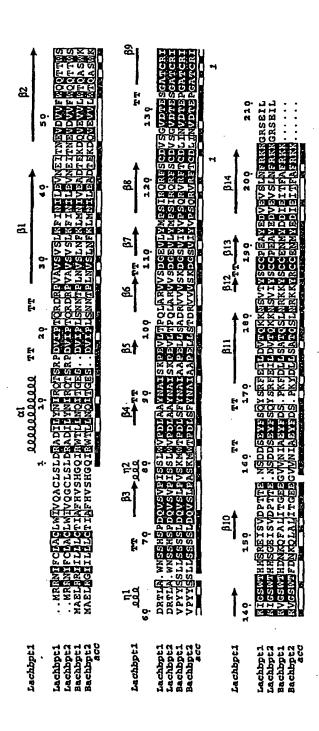


Figure 10

(15/19)

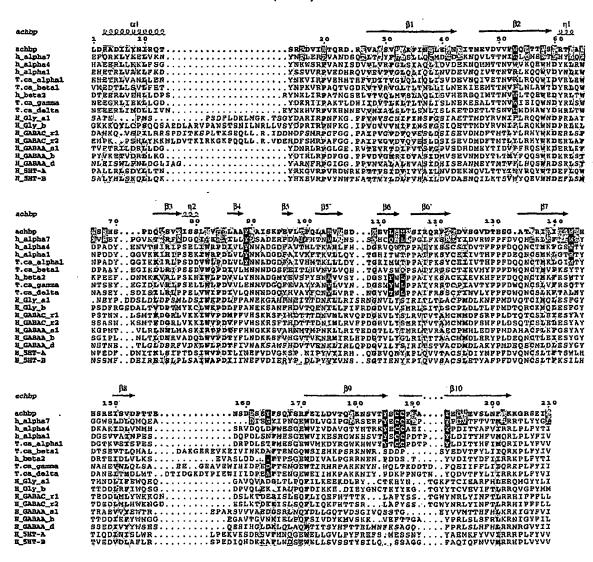


Figure 11

(16/19)

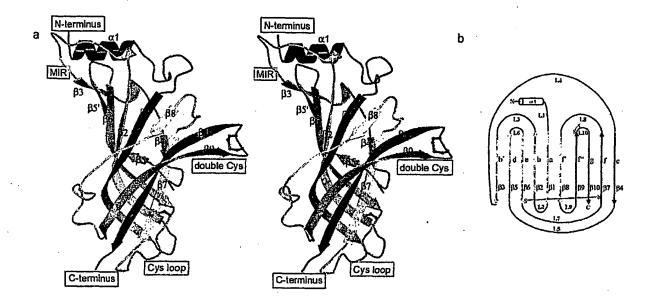


Figure 12

## (17/19)

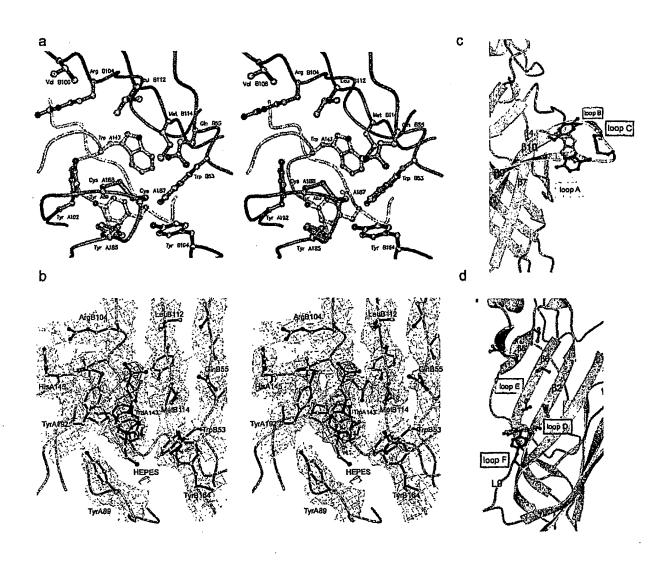


Figure 13

(18/19)

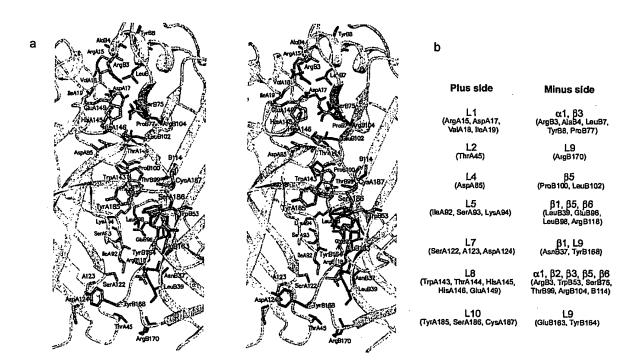


Figure 14

(19/19)

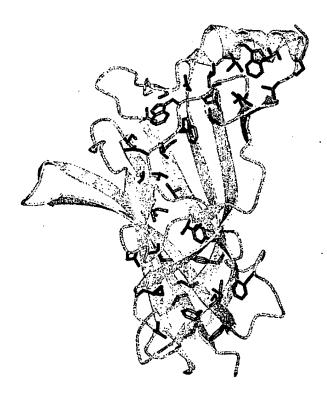


Figure 15

#### (1/20)

#### SEQUENCE LISTING

<110> Stichting voor de Technische Wetenschappen

<120> Water-soluble ligand-binding proteins and analogs of ligand-gated ion channels, crystals thereof and their use for screening ligands of ligand-gated ion channels

<130> F 1105 PCT

<140>

<141>

<160> 20

<170> PatentIn Ver. 2.1

<210> 1

<211> 690

<212> DNA

<213> Lymnaea stagnalis

<220>

<221> CDS

<222> (1)..(687)

<220>

<221> mat_peptide

<222> (58)..(687)

<400> 1

atg cgt cga aac att ttc tgc ctt gct tgt ctc tgg atc gtg caa gcg 48
Met Arg Arg Asn Ile Phe Cys Leu Ala Cys Leu Trp Ile Val Gln Ala
-15 -10 -5

tgt cta agc ttg gac cgg gca gac atc ttg tac aac ata cgt cag aca 96 Cys Leu Ser Leu Asp Arg Ala Asp Ile Leu Tyr Asn Ile Arg Gln Thr

-1 1

5

10

# (2/20)

tcg	aga	ccg	gat	gtg	att	ccc	aca	cag	cga	gat	cgc	cca	gtg	gcg	gtg	144
Ser	Arg	Pro	Asp	Val	Ile	Pro	Thr	Gln	Arg	Asp	Arg	Pro	٧al	Ala	Val	
	15					20					25					•
tcc	gtc	tct	ttg	aag	ttc	atc	aac	atc	ttg	gaa	gtg	aat	gaa	ata	acc .	192
			Leu													
30					35					40					45	
aat	gaa	gtg	gac	gtg	gtc	ttt	tgg	cag	cag	acq	aca	taa	tca	gac	асс	240
			Asp													
			_	50			-		55				551	60	9	
									-					00		
acc	ctc	gcc	tgg	aac	agt	tct	cac	tca	cca	gat	cag	at t	tee	ata	cca	288
			Trp													
			65					70		-125			75	V CL L	110	
								, 0					, ,			
ata	agc	tct	ttg	tag	gtg	cct	gac	ctc	act	σca	tac	aac	מככ	atc	tca	336
			Leu													330
		80		-			85				-1-	90			DCL	
												,,				
aaa	cct	gaa	gtc	ctt	aca	ccq	caa	cta	acc	agg	atc	αta	tcc	gat	aat	384
			Val													304
	95		•	_		100				9	105	val	501	1101	Giy	
		•														
gaa	gtg	ctg	tac	atg	ccq	agt	atc	cac	caσ	caa	ttc	tcc	tac	αat	αta	432
			Tyr													130
110			-		115			5		120		501	CJ D	1102	125	
										120					123	
tcg	ggt	gtc	gat	acg	gag	tcc	aat	act	aca	tat	caa	atc	aaa	att	aat	480
			Asp													100
			_	130			-		135	-4 -	<b>3</b>			140	013	
														140		
tcc	tgg	acc	cac	cac	aqt	aga	gag	att	tct	αta	gat	ccc	aca	aca	gaa	528
			His													220
	•		145			9		150	DC1	var	ւաբ	110		1111	GIU	
								-50					155			
aat	aot	σat:	gat	tot	gaa	tac	the	tee	caa	tac	tat		+++	man.	atc	576
			Asp													5/b
		160	بر		Jiu	- 3 -	165	261	GILL	TAT	ner		FIIE	GIU	тте	
		T00	•				103					170				

(3/20)

ttg gac gtc aca cag aag aac tcg gtt acc tac tct tgc tgt ccg 624 Leu Asp Val Thr Gln Lys Lys Asn Ser Val Thr Tyr Ser Cys Cys Pro 175 180 185 gag gca tac gag gac gtt gaa gtg agt ctc aat ttc cgg aag aag gga 672 Glu Ala Tyr Glu Asp Val Glu Val Ser Leu Asn Phe Arg Lys Lys Gly 190 195 200 205 cgc tcc gaa att ctt tag 690 Arg Ser Glu Ile Leu 210 <210> 2 <211> 229 <212> PRT <213> Lymnaea stagnalis <400> 2 Met Arg Arg Asn Ile Phe Cys Leu Ala Cys Leu Trp Ile Val Gln Ala -15 -10 -5 Cys Leu Ser Leu Asp Arg Ala Asp Ile Leu Tyr Asn Ile Arg Gln Thr -1 1 5 10 Ser Arg Pro Asp Val Ile Pro Thr Gln Arg Asp Arg Pro Val Ala Val 15 20 Ser Val Ser Leu Lys Phe Ile Asn Ile Leu Glu Val Asn Glu Ile Thr 30 35 40 Asn Glu Val Asp Val Val Phe Trp Gln Gln Thr Thr Trp Ser Asp Arg 50 55 60 Thr Leu Ala Trp Asn Ser Ser His Ser Pro Asp Gln Val Ser Val Pro 65 70 75 Ile Ser Ser Leu Trp Val Pro Asp Leu Ala Ala Tyr Asn Ala Ile Ser 80 85 90

#### (4/20)

Lys Pro Glu Val Leu Thr Pro Gln Leu Ala Arg Val Val Ser Asp Gly 95 100 105

Ser Gly Val Asp Thr Glu Ser Gly Ala Thr Cys Arg Ile Lys Ile Gly
130 135 140

Ser Trp Thr His His Ser Arg Glu Ile Ser Val Asp Pro Thr Thr Glu 145 150 155

Asn Ser Asp Asp Ser Glu Tyr Phe Ser Gln Tyr Ser Arg Phe Glu Ile 160 165 170

Leu Asp Val Thr Gln Lys Lys Asn Ser Val Thr Tyr Ser Cys Cys Pro 175 180 185

Glu Ala Tyr Glu Asp Val Glu Val Ser Leu Asn Phe Arg Lys Lys Gly
190 200 205

Arg Ser Glu Ile Leu 210

<210> 3

<211> 690

<212> DNA

<213> Lymnaea stagnalis

<220>

<221> CDS

<222> (1)..(687)

<220>

<221> mat_peptide

<222> (58)..(687)

<400> 3

## (5/20)

atg	cgt	cga	aac	att	ttc	tgc	ctt	gct	tgt	ctc	tgg	atc	gtg	caa	ggg	48
Met	Arg	Arg	Asn	Ile	Phe	Cys	Leu	Ala	Cys	Leu	Trp	Ile	Val	${\tt Gln}$	Gly	
				-15					-10					~5		
tgt	cta	agc	ttg	gac	cgg	gca	gac	atc	ttg	tac	aac	ata	cgt	cag	aca	96
Cys	Leu	Ser	Leu	qaA	Arg	Ala	Asp	Ile	Leu	Tyr	Asn	Ile	Arg	Gln	Thr	
		-1	1				5					. 10				
										•						
tcg	aga	ccg	gat	gtg	att	ccc	aca	cag	cga	gat	cgc	cca	gtg	gcg	gtg	144
Ser	Arg	Pro	Asp	Val	Ile	Pro	Thr	Gln	Arg	Asp	Arg	Pro	Val	Ala	Val	
	15					. 20				-	25					
tcc	gtc	tct	ttg	aag	ttc	atc	aac	atc	ttg	gaa	gtg	aat	gaa	ata	acc	192
Ser	Val	Ser	Leu	Lys	Phe	Ile	Asn	Ile	Leu	Glu	Val	Asn	Glu	Ile	Thr	
30					35					40					45	
						•										
aat	gaa	gtg	gac	gtg	gtc	ttt	tgg	cag	cag	acg	aca	tgg	tcg	gac	agg	240
Asn	Glu	Val	Asp	Val	Val	Phe	Trp	Gln	Gln	Thr	Thr	Trp	Ser	Asp	Arg	
				50					55					-60		
acc	ctc	gcc	tgg	aac	agt	tct	cac	tca	cca	gat	cag	gtt	tcc	gtg	cca	288
			Trp													
			65					70					75			
															•	
ata	agc	tct	ttg	tgg	gtg	cct	gac	ctc	gct	gca	tac	aac	gcc	atc	tcg	336
			Leu												_	
		80					85				-	90				
aaa	cct	gaa	gtc	ctt	aca	ccg	caa	ctg	gcc	agg	gtc	gta	tcc	gat	gat	384
			Val													
	95					100				_•	105			•	•	
gaa	gtg	ctg	tac	atg	ccg	agt	atc	cgc	cag	caa	ttc	tcc	tac	gat	qta	432
			Tyr													
110			_		115			7		120					125	
															-	
cg	ggt	gtc	gat	acg	gag	tcc	ggt	gct	acg	tgt	cgg	atc	aaa	att	ggt	480
			Asp													
	-		-	130			-		135	-				140	4	
									_							

#### (6/20)

tcc tgg acc cac cac agt gga gag att tct gta gat ccc acg aca gaa Ser Trp Thr His His Ser Gly Glu Ile Ser Val Asp Pro Thr Thr Glu 145 150 155 aat agt gat gat tot gaa tac ttc tcc caa tac tct cgc ttt gaa atc Asn Ser Asp Asp Ser Glu Tyr Phe Ser Gln Tyr Ser Arg Phe Glu Ile 160 165 170 ttg gac gtc aca cag aag aac tcg gtt atc tac tct tgc tgt ccg Leu Asp Val Thr Gln Lys Lys Asn Ser Val Ile Tyr Ser Cys Cys Pro 175 180 185 gag gca tac gag gac gtt gaa gtg agt ctc aat ttc cgg aag aag gga 672 Glu Ala Tyr Glu Asp Val Glu Val Ser Leu Asn Phe Arg Lys Lys Gly 190 195 200 205 cgc tcc gaa att ctt tag 690 Arg Ser Glu Ile Leu 210 <210> 4 <211> 229 <212> PRT <213> Lymnaea stagnalis <400> 4 Met Arg Arg Asn Ile Phe Cys Leu Ala Cys Leu Trp Ile Val Gln Gly -15 -10 -5 Cys Leu Ser Leu Asp Arg Ala Asp Ile Leu Tyr Asn Ile Arg Gln Thr -1 1 . 5 10 Ser Arg Pro Asp Val Ile Pro Thr Gln Arg Asp Arg Pro Val Ala Val 15 20 25 Ser Val Ser Leu Lys Phe Ile Asn Ile Leu Glu Val Asn Glu Ile Thr 30 40

Asn Glu Val Asp Val Val Phe Trp Gln Gln Thr Thr Trp Ser Asp Arg

(7/20)

50

55

60

Thr Leu Ala Trp Asn Ser Ser His Ser Pro Asp Gln Val Ser Val Pro 65 70 75

Ile Ser Ser Leu Trp Val Pro Asp Leu Ala Ala Tyr Asn Ala Ile Ser 80 85 90

Lys Pro Glu Val Leu Thr Pro Gln Leu Ala Arg Val Val Ser Asp Gly
95 100 105

Ser Gly Val Asp Thr Glu Ser Gly Ala Thr Cys Arg Ile Lys Ile Gly 130 135 140

Ser Trp Thr His His Ser Gly Glu Ile Ser Val Asp Pro Thr Thr Glu 145 150 155

Asn Ser Asp Asp Ser Glu Tyr Phe Ser Gln Tyr Ser Arg Phe Glu Ile 160 165 170

Leu Asp Val Thr Gln Lys Lys Asn Ser Val Ile Tyr Ser Cys Cys Pro 175 180 185

Arg Ser Glu Ile Leu

210

<210> 5

<211> 675

<212> DNA

<213> Bulinus truncatus

<220>

# (8/20)

<22	1> C	DS														
<22	2> (	1)	(672	)												
<22	0>															
<22	1> m	at_p	epti	de												
<222> (64)(672)																
<40	0> 5			•								,				
atg	gct	gaa	cta	cga	agg	atc	att	ctt	ctg	cta	tgt	act	att	gcc	ttt	48
Met	Ala	Glu	Leu	Arg	Arg	Ile	Ile	Leu	Leu	Leu	Cys	Thr	Ile	Ala	Phe	
	-20					-15					-10					
			cat													96
His	Val	Ser	His	Gly	Gln	Ile	Arg	Trp	Thr	Leu	Leu	Asn	Gln	Ile	Thr	
-5				-1	1				5					10		
ggt	gaa	tct	gac	gtc	att	ccg	ctg	tct	aac	aac	acg	ccc	ctg	aat	gtg	144
			Ąsp													
			15					20					25			,
tcg	ctg	aat	ttt	aag	ctg	atg	aat	atc	gta	gag	gcg	gac	aca	gaa	aaa	192
			Phe													
		30					35					40			-1-	
			gag													240
Asp	45	vaı	Glu	Val	Val		Trp	Thr	Gln	Ala		Trp	Lys	Val	Pro	
	45					50					55					
tat	tac	agc	tca	ctg	ctg	tcc	tct	agc	agt	tta	gac	cag	gtg	agc	tta	288
Tyr	Tyr	Ser	Ser	Leu	Leu	Ser	Ser	Ser	Ser	Leu	Asp	Gln	Val	Ser	Leu	
60				٠	65					70					75	
cca	gtc	agc	aaa	atg	tgg	acc	cca	gac	ctt	tct	ttc	tac	aac	gcc	atc	336
Pro	Val	Ser	Lys	Met	Trp	Thr	Pro	qaA	Leu	Ser	Phe	Tyr	Asn	Ala	Ile	
				80				•	85					90		
gct	gca	ccc	gag	ttg	ctc	tcc	gca	gac	cgc	gta	gta	gtc	tct	aao	gac	384
			Glu													
			95					100	ŭ	-			105			

## (9/20)

		Val	att Ile													432
		110					115	-			•	120				
			gtc Val													480
	125					130					135					
			acc													528
140	per	rrp	Thr	nis	145	ASN	гув	GIN	Pue	150	ьеи	TTE	Thr	GIĀ	155	
gag	ggg	gtg	gtg	aat	att	gca	gag	, tac	ttc	gac	agc	cca	aag	ttt	gac	576
Glu	Gly	Val	Val	Asn 160	Ile	Ala	Glu	Tyr	Phe 165	Asp	Ser	Pro	Lys	Phe	Asp	
a++		a ~ h	~													<b>.</b>
			gcc Ala													624
			175					180					185			
			tat Tyr													672
-		190	- 7 -	Nop		116	195	116	1111	FIIC	ATA	200	Arg	гуз	тйя	
taa																675
•																
<210	)> 6 -> 22	24														
<212	?> PF	T														
<213	i> Bu	ılinu	ıs tr	unca	atus											
<400 Met		Glu	Leu	Ara	Arα	Tle	Tle	Len	Leu	Len	Cva	መከጉ	Tla	λla	Pho	
	-20			9	5	-15			204	-cu	-10	****	116	nia	·	
	Val	Ser	His		Gln	Ile	Arg	Trp	Thr	Leu	Leu	Asn	Gln	Ile	Thr	
-5				-1	1				5		•			10		
Gly	Glu	Ser	Asp	Val	Ile	Pro	Leu	Ser	Asn	Asn	Thr	Pro	Leu	Asn	Val	

#### (10/20)

Ser	Leu	Asn	Phe	Lys	Ļeu	Met	Asn	Ile	Val	Glu	Ala	Asp	Thr	Glu	Lys
		30					35					40			

Asp Gln Val Glu Val Val Leu Trp Thr Gln Ala Ser Trp Lys Val Pro
45 55 *

Tyr Tyr Ser Ser Leu Leu Ser Ser Ser Ser Leu Asp Gln Val Ser Leu 60 65 70 75

Pro Val Ser Lys Met Trp Thr Pro Asp Leu Ser Phe Tyr Asn Ala Ile 80 85 90

Ala Ala Pro Glu Leu Leu Ser Ala Asp Arg Val Val Val Ser Lys Asp 95 100 105

Gly Ser Val Ile Tyr Val Pro Ser Gln Arg Val Arg Phe Thr Cys Asp 110 115 120

Leu Ile Asn Val Asp Thr Glu Pro Gly Ala Thr Cys Arg Ile Lys Val 125 130 135

Gly Ser Trp Thr His Asp Asn Lys Gln Phe Ala Leu Ile Thr Gly Glu 140 145 150 155

Glu Gly Val Val Asn Ile Ala Glu Tyr Phe Asp Ser Pro Lys Phe Asp 160 165 170

Leu Leu Ser Ala Thr Gln Ser Leu Asn Arg Lys Lys Tyr Ser Cys Cys
175 180 185

Glu Asn Met Tyr Asp Asp Ile Glu Ile Thr Phe Ala Phe Arg Lys Lys 190 195 200

<210> 7

<211> 675

<212> DNA

## (11/20)

<21	3> B	ulin	us t	runc	atus	1										
<22	0>															
<22	1> C	DS														
<22	2> (	1)	(672	)												
<22																
<22	1> m	at_p	epti	de												
<22	2> (	64).	. (67	2)									,			,
<40	0> 7															
atg	gct	gaa	cta	cga	ggg	atc	att	ctt	ctg	cta	tgt	act	att	gcc	ttt	48
Met	Ala	Glu	Leu	Arg	Gly	Ile	Ile	Leu	Leu	Leu	Cys	Thr	Ile	Ala	Phe	
	-20					-15		•			-10					
cat	gtt	tcc	cat	gga	caa	ata	aga	taa	aco	cta	cta	aat	can	atc	acc	96
			His													50
-5				-1			_	_	5					10		
ggt	gaa	tct	gac	gtc	att	ccg	ctg	tct	aac	aac	acg	cca	ctg	aat	gtg	144
Gly	Glu	Ser	Asp	Val	Ile	Pro	Leu	Ser	Asn	Asn	Thr	Pro	Leu	Asn	Val	
			15					20					25			
			ttt													192
Ser	Leu	Asn	Phe	Lys	Leu	Met	Asn	Ile	Leu	Glu	Ala	Ąsp	Thr	Glu	Lys	
		30			•		35					40				
gat	caa	ata	gag	atc	ata	cta	taa	aca	can	act	arc	taa	222	at a	000	240
			Glu													240
•	45					50			Ų	u	55	ינייי	د بر	Val	FIO	
		•														
tat	tac	agc	tca	ctg	ctg	tcc	tct	agc	agt	tta	gac	cag	gtg	agc	tta	288
Tyr	Tyr	Ser	Ser	Leu	Leu	Ser	Ser	Ser	Ser	Leu	Asp	Gln	Val	Ser	Leu	
60					65					70					75	
			aaa		,											336
Pro	Ala	Ser	Lys	Met	Trp	Thr	Pro	Asp	Leu	Ser	Phe	Tyr	Asn	Ala	Ile	
				80					85					90		
gct	σca	CCC	σaσ	tta	ata	tcc	aca	u a c	ccc	ata	ata	ata	tat	224	~~~	301

.

## (12/20)

Ala	Ala	Pro	Glu	Leu	Leu	Ser	Thr	Asp	Arg	Val	Val	Val	Ser	Lys	Asp	
			95					100					105			
					gtg											432
Glу	Ser	Val	Ile	Tyr	Val	Pro	Ser	Gln	Arg	Val	Arg	Phe	Thr	Cys	Asp	
		110					115					120				
			٠													
•					acg											480
Leu		Asn	Val	Asp	Thr		Pro	Gly	Ala	Thr		Arg	Ile	Lys	Val	
	125					130					135					
																500
					gac									_	_	528
	Ser	Trp	Thr	Phe	Asp	Asn	ьуs	Gin	Leu		Leu	тте	Thr			
140					145					150					155	
	****				_ 4. 4.	~~~	~~~	<b>+</b>	<b>+</b> + ~	~~~	.~.		224	+24	<b>434</b>	576
			-		att Ile											370
GIU	GIY	Val	Vai	160	116	ALG	GIU	тÄт	165	rsp	Per	FLO	пуъ	170	ASP	
				100					103					1,0		
ctt	tta	ant	acc	aca	cag	aαt	cta	aat	cac	aaq	aaα	tac	aσa	tat	tac	624
	•	•	-		Gln	-	_		_	_	_		_			
			175					180					185	•		
gag	aat	atg	tat	gaa	gac	att	gaa	att	acc	ttt	gca	ttc	aga	aag	aag	672
					Asp											
٠		190					195					200				
taa									•						•	675
<21	0> 8															
<21	1> 2	24														
<21	2> P	RT														
<21	3> B	ulin	us t	runc	atus									•		
	0> 8															
Met	Ala	Glu	Leu	Arg	Gly			Leu	Leu	Leu		Thr	Ile	Ala	Phe	
	-20					-15					-10					
						_			_	_	_	_				
His	Val	Ser	His	Gly	Gln	Ile	Arg	$\mathtt{Trp}$	Thr	Leu	Leu	Asn	GIn	Ile	Thr	

## (13/20)

-5				-1	1				5					10	
Gly	Glu	Ser	Asp 15		Ile	Pro	Leu	Ser 20	Asn	Asn	Thr	Pro	Leu 25		Va:
Ser	Leu	Asn 30	Phe	Lys	Leu	Met	Asn 35	Ilę	Leu	Glu	Ala	Asp 40	Thr	Glu	Lys
Asp	Gln 45	Val	Glu	Val	Val	Leu 50	Trp	Thr	Gln	Ala	Ser 55	Trp	Lys	Val	Pro
Туr 60	Tyr	Ser	Ser	Leu	Leu 65	Ser	Ser	Ser	Ser	Leu 70		Gln	Val	Ser	Leu 75
Pro	Ala	Ser	Lys	Met 80	Trp	Thr	Pro	Asp	Leu 85	Ser	Phe	Tyr	Asn	Ala 90	Ile
Ala	Ala	Pro	Glu 95	Leu	Leu	Ser	Thr	Asp 100	Arg	Val	Val	Val	Ser 105	Lys	Asp
Gly	Ser	Val 110	Ile	Tyr	Val	Pro	Ser 115	Gln	Arg	Val	Arg	Phe 120	Thr	Cys	Asp
Leu	Ile 125	Asn	Val	Asp	Thr	Glu 130	Pro	Gly	Ala	Thr	Суs 135	Arg	Ile	Lys	Val
Gly 140	Ser	Trp	Thr	Phe	Asp 145	Asn	Lys	Gln	Leu	Ala 150	Leu	Ile	Thr	Gly	Glu 155
Glu	Gly	Val	Val	Asn 160	Ile	Ala	Glu	Туг	Phe 165	Asp	Ser	Pro	Lys	Туr 170	Asp
Leu	Leu	Ser	Ala 175	Thr	Gln	Ser	Leu	Asn 180	Arg	Lys	Lys	Tyr	Arg 185	Cys	Сув
Glu .		Met 190	Tyr	Glu	Asp	Ile	Glu 195	Ile	Thr	Phe	Ala	Phe 200	Arg	Lys	Ьуз

d

(14/20)

<210> 9	
<211> 502	
<212> PRT	
<213> Homo sapiens	
<220>	
<221> DOMAIN	
<222> (1)(235)	
<400> 9	
Met Arg Cys Ser Pro Gly Gly Val Trp Leu Ala Leu Ala Ala Ser L	eu .
1 5 10 15	
Leu His Val Ser Leu Gln Gly Glu Phe Gln Arg Lys Leu Tyr Lys G	lu
20 25 30	
Leu Val Lys Asn Tyr Asn Pro Leu Glu Arg Pro Val Ala Asn Asp S	er .
35 40 45	
Gln Pro Leu Thr Val Tyr Phe Ser Leu Ser Leu Leu Gln Ile Met A	สอ
50 55 60	رړد
Val Asp Glu Lys Asn Gln Val Leu Thr Thr Asn Ile Trp Leu Gln M	et.
CF.	80
	,
Ser Trp Thr Asp His Tyr Leu Gln Trp Asn Val Ser Glu Tyr Pro G	lv
85. 90 95	-1
Val Lys Thr Val Arg Phe Pro Asp Gly Gln Ile Trp Lys Pro Asp I	ie
100 105 110	
Leu Leu Tyr Asn Ser Ala Asp Glu Arg Phe Asp Ala Thr Phe His T	ır
115 120 125	-
Asn Val Leu Val Asn Ser Ser Gly His Cys Gln Tyr Leu Pro Pro G	iν
130 135 140	-3

## (15/20)

Val	Gln	His	Суз	Lуз 165	Leu	Lys	Phe	Gly	Ser 170	Trp	Ser	Tyr	Gly	Gly 175	Trp
Ser	Leu	Asp	Leu 180	Gln	Met	Gln	Glu	Ala 185	Asp	Ile	Ser	Gly	Tyr 190	Ile	Pro
Asn	Gly	Glu 195	Trp	Asp	Leu	Val	Gly 200	Ile	Pro	Gly	Ĺys	Arg 205	Ser	Glu	Arg
Phe	Туг 210	Glu	Cys	Сув	Lys	Glu 215	Pro	Tyr	Pro	Asp	Val 220	Thr	Phe	Thr	Val
Thr 225	Met	Arg	Arg	Arg	Thr 230	Leu	Tyr	Tyr	Gly	Leu 235	Asn	Leu	Leu	Ile	Pro
Сув	Val	Leu	Ile	Ser 245	Ala	Leu	Ala	Leu	Leu 250	Val	Phe	Leu	Leu	Pro 255	Ala
qa <i>l</i>	Ser	Gly	Glu 260	Lys	Ile	Ser	Leu	Gly 265	Ile	Thr	Val	Leu	Leu 270	Ser	Leu
Thr	Val	Phe 275	Met	Leu	Leu	Val	Ala 280	Glu	Ile	Met	Pro	Ala 285	Thr	Ser	Asp
Ser	Val 290	Pro	Leu	Ile	Ala	Gln 295	Tyr	Phe	Ala	Ser	Thr 300	Met	Ile	Ile	Val
31y 305	Leu	Ser	Val	Val	Val 310	Thr	Val	Ile	Val	Leu 315	Gln	Tyr	His	His	His 320
/sp	Pro	Asp	Gly	Gly 325	Lys	Met	Pro	Lys	Trp 330	Thr	Arg	Val	Ile	Leu 335	Leu
lsn	Trp	Cys	Ala 340	Trp	Phe	Leu	Arg	Met 345	Lys	Arg	Pro	Gly	Glu 350	Asp	Lys
/al	Arg	Pro 355	Ala	Cys	Gln	His	Lys 360	Gln	Arg	Arg	Cys	Ser 365	Leu	Ala	Ser
7a l	Gliv	Mat	Sar	77.5	₹72 T	אן א	Dvc	Dwc	Dwe	או ה	C-~	7	<b>~1.</b>	*	<b>.</b>

(16/20)

370

375

380

Leu Tyr Ile Gly Phe Arg Gly Leu Asp Gly Val His Cys Val Pro Thr 385 390 395 400

Pro Asp Ser Gly Val Val Cys Gly Arg Met Ala Cys Ser Pro Thr His
405 410 415

Asp Glu His Leu Leu His Gly Gly Gln Pro Pro Glu Gly Asp Pro Asp
420 425 430

Leu Ala Lys Ile Leu Glu Glu Val Arg Tyr Ile Ala Asn Arg Phe Arg 435 440 445

Cys Gln Asp Glu Ser Glu Ala Val Cys Ser Glu Trp Lys Phe Ala Ala 450 455 460

Cys Val Val Asp Arg Leu Cys Leu Met Ala Phe Ser Val Phe Thr Ile 465 470 475 480

Ile Cys Thr Ile Gly Ile Leu Met Ser Ala Pro Asn Phe Val Glu Ala
485 490 495

Val Ser Lys Asp Phe Ala 500

<210> 10

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: N-terminus of mature LAChBP1

<400> 10

Leu Asp Arg Ala Asp Ile Leu Tyr Asn Ile

1

5

10

#### (17/20)

```
<210> 11
<211> 32
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:
      Oligonucleotides encoding N-terminal peptide of
      LAChBP1
<220>
<221> modified_base
<222> (13)
<223> i
<400> 11
                                                                   32
cggatccgay mgagcngaya thytntayaa ya
<210> 12
<211> 31
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer1 useful
      for cloning cDNA encoding LAChBP (optionally with
      Primer2)
<220>
<221> modified_base
<222> (14)
<223> i
<220>
<221> modified_base
<222> (20)
<223> i
```

.

(18/20)

```
<400> 12
gcgaattcga yacagarwsa ggngcnacnt g
                                                                  31
<210> 13
<211> 33
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer2
      useful for cloning cDNA encoding LAChBP
      (optionally with Primer1)
<220>
<221> modified_base
<222> (20)
<223> i
<400> 13
gcgaagcttc rtcytcrtaa gcytcngcrc arc
                                                                   33
<210> 14
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: His-tag
<400> 14
Ser Arg Gly His His His His His
 1
<210> 15
<211> 14
<212> PRT
<213> Artificial Sequence
```

#### (19/20)

<220> <223> Description of Artificial Sequence: His-tag <400> 15 Glu Phe Lys Asp Asp Asp Lys His His His His His 10 <210> 16 <211> 4 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Additional amino acids at the N-terminus of mature LAChBP due to alpha-mating factor cleavage site <400> 16 Glu Ala Glu Ala 1 <210> 17 <211> 47 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Primer useful for generating LAChBP/alpha7 nAChR chimera <400> 17 gcgctcgaga aaagagaggc tgaagctttg gaccgggcag acatctt 47 <210> 18 <211> 30

<212> DNA

#### (20/20)

12131	racificial polynomes	
<220>		
<223>	Description of Artificial Sequence: Primer useful	
	for generating LAChBP/alpha7 nACHR chimera	
<400>	18	
cgcgaa	attca agaatttcgg agcgtccctt	30
<210>		
<211>		
<212>		
<213>	Artificial Sequence	
.000		
<220>	Describbles of Authorities of a second	
<223>	Description of Artificial Sequence: Primer useful	
	for generating LAChBP/alpha7 nACHR chimera	
<400>	19	
	aacca gacattotoo totacaacgo catotogaaa oo	42
5-55		
<210>	20	
<211>	39	
<212>	DNA	
<213>	Artificial Sequence	
<220>		
<223>	Description of Artificial Sequence: Primer useful	
	for generating LAChBP/alpha7 nACHR chimera	
<400>	·	
gaggag	gaatg tetggtttee acaaagaget tattggeae	39

# This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

#### **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:
BLACK BORDERS
☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
☐ FADED TEXT OR DRAWING
☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
☐ SKEWED/SLANTED IMAGES
COLOR OR BLACK AND WHITE PHOTOGRAPHS
☐ GRAY SCALE DOCUMENTS
LINES OR MARKS ON ORIGINAL DOCUMENT
☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

# IMAGES ARE BEST AVAILABLE COPY.

☐ OTHER:

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.